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## THE EVOLUTION OF INFECTIOUS DISEASES IN THE COURSE OF HISTORY\*

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IN THE NOT TOO DISTANT past all over the world, large numbers of children died during the first years of infancy. According to Hugh Smith in *The Family Physician*, approximately two-thirds of London's children born between 1762 and 1771 died before the age of five, and fully three-quarters of them never reached the age of two. Queen Anne provides a notorious illustration of this tragic past, with 17 pregnancies and not a single surviving child. The situation is very different today in the Western World. Largely through the control of microbial diseases and the improvements in general nutrition, the immense majority of children now survive. In this lecture dedicated to the memory of a great paediatrician it would be proper, therefore, to emphasize the spectacular contributions made by modern medicine to the welfare of children. Instead, I have considered it more profitable to discuss before you some of the new problems of infection that are likely to arise in the future as a result of biological and social changes. My theme is that the incidence, character and severity of microbial diseases have varied from one generation and from one type of civilization to another, and that the experience gained in the past will not necessarily provide all the answers to the problems of their control in the future.

Writing of syphilis in the second volume of *De Contagione*, Fracastoro asserted that "while the contagion is still flourishing today, it seems to have changed its character since those earliest periods of its appearance. I mean that, within the last twenty years or so, fewer pustules began to appear, but more gummata, whereas the contrary had been the case in the earlier years. . . . There will come yet other new and unusual ailments, as time brings them in its course. . . . This disease of which I speak, this syphilis, too will pass away and die out, but later it will be born again and be seen again by our grandchildren." In the poem *Syphilis sive Morbus Gallicus* Fracastoro prayed

Apollo to preserve his writings "because our descendants may one day like to read of the signs and appearance of this disease. It will come again."

During the past two centuries, many clinicians, epidemiologists, and experimenters have followed Fracastoro in believing that infectious diseases can exhibit natural ebbs and flows. As Charles Nicolle claimed in his famous book, the "*Naissance, vie, et mort des maladies infectieuses*" constitute events that are often governed by forces independent of conscious human intervention.

At first sight it appears that in reality diseases have changed little, if any, in the course of time. Indeed, the study of prehistoric bones and of mummies shows that most of the diseases presently known did occur in ancient civilizations and even before the dawn of history. But what has changed is the relative incidence and severity of these diseases. Many examples come to mind to illustrate this thesis. Leprosy was very prevalent in Europe during the Middle Ages, and yet disappeared as it were spontaneously during the 16th century without the conscious use of any therapeutic or control procedures. Likewise, the notorious "sweating sicknesses" which caused several dramatic outbreaks during Tudor times, disappeared from the European stage as suddenly and mysteriously as it had made its appearance, although it may continue to lurk in the background under the guise of mild virus infections. As to influenza, its vagaries are apparent to all, and the great pandemics of 1896 and 1918 leave the world in fear of a resurgence of the killing form of the disease. Granted that retrospective diagnoses of ancient epidemics are at best uncertain, it may be useful to review briefly some of the historical accounts of scarlet fever, measles and tuberculosis that have come to us from distinguished physicians of the past.

In a book printed in 1701, scarlet fever was referred to as "this Name of a disease, for it is scarce anything more". A century and a half later, however, Graves took a different view of the subject. "In the year 1801," he wrote, "scarlet fever committed great ravages in Dublin, and continued its destructive progress during the spring of 1802. It ceased in summer, but returned at intervals during the years 1803-4, when the disease changed its character . . . either so mild as to require little care or so purely inflammatory as to yield readily to the judicious employment of an antiphlogistic treatment. . . . The experience derived

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from the present epidemic (1834-5) . . . has proved that, in spite of our boasted improvements, we have not been more successful in 1834-5 than were our predecessors in 1801-2." In 1840 scarlet fever suddenly doubled its mortality in England and Wales. From then until 1880 it was the chief cause of death amongst the infectious maladies of childhood, and accounted for 4 to 6% of deaths at all ages. The highest mortality from the disease in England was reached apparently during the period 1861-70. In 1863 the death rate from scarlet fever was 1500 per million. Of every million children born in Liverpool at that time, some 27,000 died of the infection before attaining the age of five. After this devastating spell, the severity of scarlet fever declined and, by 1900, first measles and then diphtheria surpassed it as a cause of death. As is well known, scarlet fever retained nevertheless some of its malignancy until the beginning of the present century. It was then the fever and, to use Major Greenwood's words, it did not require a qualifying adjective any more than the plague does. More recently scarlet fever has again become a relatively mild disease. Indeed, it is probable that much of the credit for its control commonly given to improved methods of treatment (as was done at the beginning of the last century) should in reality go to the unknown factors which brought about its "spontaneous" decrease in virulence.

A similar story can be told of the fluctuations in the severity of measles. Heberden asserted in 1785 that measles are "usually attended with very little danger; it is not often that a physician is employed in this distemper." But the position changed sharply about 1800. In 1804 measles caused as many deaths, chiefly among adults, as did smallpox, and actually surpassed the latter in 1808. The illness appears to have resembled what Sydenham in 1674 called "anomalous" or "malignant" measles and it is probable that its mortality was even greater than indicated by statistics, since it must have caused many fatal chest affections that went undiagnosed. Measles remained the leading cause of child deaths until around 1840; then it began to ebb, and scarlet fever displaced it for over 40 years as the chief infectious disease. But towards the end of the century measles again resumed some of its importance and almost every year until 1915 the deaths from it outnumbered those from smallpox, scarlet fever and diphtheria combined. From then on its mortality fell and it has continued to fall ever since.

Tuberculosis, as everyone knows, was the most important cause of disease and death among young adults during the early part of the 19th century. But the annual tuberculosis mortality, which was approximately 500 per 100,000 population at that time over much of the Western World, decreased during the second half of the century. In many places it fell to 200 in 1900 and to less than 50

in 1945 — long before vaccination or chemotherapy could have had an influence on the evolution of the disease.

The medical history of the Polynesians, the Amerindians, the Africans, and the Eskimos has provided dramatic examples of the ferocity of certain microbial diseases when first brought to these peoples by the white man. Suffice it to mention for illustration that when measles was first introduced into Hawaii practically the whole population went down with the disease. Further epidemics of measles, influenza and pertussis struck Hawaii again in 1848 and every child born that year died. In 1853, there were over 9000 cases of smallpox with 6000 deaths out of a population of 70,000.

While the microbial diseases introduced by the white man proved at first so immensely destructive among people formerly isolated, it is also true that these diseases became progressively less virulent in the course of time. Within a few generations in many places they have taken the form of less acute processes not unlike those seen presently in the Western World. Like other manifestations of life, microbial diseases do not remain constant in time and it is the mechanism of their transformations that we shall now consider.

It would be impossible here to review the history of the views concerning the evolution of infectious diseases, but mention must be made of the fact that the theoretical basis of this subject emerged from the contributions of three men who made scientific history exactly one hundred years ago.

It was in 1858 that Darwin published the *Origin of Species*. Even though Darwin made but few mentions of disease, it was implicit in the theory of evolution that the fitness and even the survival of a species under natural conditions in a given environment is possible only when adaptive characters result in an adequate level of resistance to the pathogens ubiquitous in this environment. The fact that new diseases take a particularly virulent form in populations unfamiliar with them is clearly a manifestation of Darwin's principle of geographical isolation. It is of interest in this regard that Darwin himself had pointed out that when different population groups are brought into contact they introduce their diseases to one another in an extremely virulent form.

The name of Rudolph Virchow—whose *Cellular Pathology* also appeared in 1858—is identified with another aspect of the epidemiology of infection. From his experience with relapsing fever in Silesia, Virchow had gained the conviction that the physical and social environments were of paramount importance in determining resistance to contagious diseases. On this basis, he taught that social and economic reforms were part of medical action because misery was the breeder of disease.

Finally this was the time when Pasteur entered the biological field, and suggested in his memoirs on fermentation that microbes would be found to

be responsible for contagious diseases. Furthermore, Pasteur recognized very early that microbes can undergo variation in many of their characteristics, and he was visionary and bold enough to suggest that changes in virulence might play a part in the genesis and evolution of epidemics.

The epidemiological concepts identified with Darwin, Virchow and Pasteur constitute the theoretical background of this lecture, but I wish to emphasize at the outset that epidemiological phenomena are probably influenced by still other determinants which do not fall into the categories referred to above. The cyclic changes that occur naturally in populations of wild birds and rodents suggest that animal behaviour and susceptibility to disease are under the control of unidentified factors. While sunspots and radiations are often mentioned presently as corresponding to some of the telluric factors of old epidemiology, it must be acknowledged that even the most modern observations on these problems do not yet lend themselves to scientific understanding, however fascinating they may be in revealing the complexity of population changes. For this reason we shall not discuss them further, but we must nevertheless remain aware of the likelihood that many interesting aspects of the epidemic climate will not be accounted for by present scientific doctrines.

Changes in environmental conditions, in the virulence of the parasite, and in susceptibility of the host, all play a role in the spontaneous fluctuations in epidemic diseases. We shall deal with these factors separately even though they are, of course, interrelated and cannot readily be separated in actual practice.

It is certain that in the case of man social and cultural forces have greatly influenced the course of infectious diseases during historical times. At first blindly and empirically, then more and more rationally, man has developed sanitary rules for camp life as well as practices of vaccination which have helped to minimize the effects of infection. Furthermore, the ancient belief that war, famine, and pestilence ride together was a manifestation of awareness that the general standard of living, and the state of nutrition in particular, profoundly affect the resistance of man to his potential pathogens. But while history provides many examples illustrating the relation of wars and social upheavals to the spread and severity of epidemics, the effects of long-trend social factors on the evolution of microbial disease are far more difficult to establish and to separate from those resulting from the operation of blind biological forces.

The biological forces involving the virulence of microbes are somewhat better understood. Ever since Pasteur, it has been known that microbes can undergo genetic alterations which modify their pathogenic behaviour, and it has been suspected that increase in virulence as well as changes in immunological specificity can result in the initiation of new epidemics. On the other hand, de-

creases in virulence can also occur under certain circumstances and it was legitimate to surmise that this type of change might be of practical importance under natural conditions. The knowledge recently derived from the study of rabbit myxomatosis in Australia provides a well-documented example of decrease of virulence in the course of an epidemic.

The European rabbit was introduced around 1860 in Australia where it multiplied enormously and soon became an economic plague. In an attempt to control it, the virus of myxomatosis was released on the Australian continent because this disease was known to be almost uniformly fatal in laboratory rabbits. The initial outbreaks of myxomatosis in Australia were characterized by an enormously high case mortality rate—higher than 99%. Within a year, however, the case mortality had fallen to 90% in areas where a second spontaneous outbreak had occurred. This fall was apparently due in part to a decrease in the virulence of the virus. In Australia, the virus is transmitted from rabbit to rabbit almost entirely through mosquitoes which act mechanically as "flying needles". Because the highly virulent strain of virus killed the rabbits within a very few days, the chances for its transmission through the mosquito vector were rather limited. However, when a virus of lower virulence appeared spontaneously by mutation, it produced in the rabbit a less rapidly fatal disease, with skin lesions of longer duration. Thus the less virulent mutant strain had a better chance of being transmitted through mosquito bite and it progressively displaced in the field the original highly virulent strain. A few years after its introduction in Australia, the virus caused a mortality of 90% in European laboratory rabbits, instead of more than 99% as it had originally.

Among alterations in the host which increase resistance to infection, the most familiar and best understood are of course those resulting from prior contact of the individual with the infectious agent. It is certain that repeated exposure to small infective doses at the proper time can give rise to humoral or cellular immunity; the evidence for immunity acquired in this wise is clear in the case of influenza. There is no doubt furthermore that infections contracted during the school years—the golden period of resistance—contribute to the lasting immunity of adults to many of the so-called childhood diseases. While these phenomena related to acquired immunity are so well known as to need no further discussion here, there is another aspect of the problem which seems to have received less emphasis than it deserves, namely the genetic changes which come into play in populations exposed to generalized epidemics.

It is not easy to prove that genetic changes occur in the resistance of man to his pathogens during widespread epidemics. Nevertheless, one may postulate that since epidemics with a great killing

power tend to eliminate a large percentage of the persons possessing a high degree of susceptibility, the likely outcome is the selective survival and multiplication of the individuals endowed with a higher than average genetic resistance. This is presently taking place in Australia among rabbits surviving from the epidemic of myxomatosis. Experiments in guinea pigs, rabbits, and mice have shown that it is possible in the laboratory to select from these animal species families having genetic determinants conferring upon them a higher resistance to tuberculosis. In man also, studies of the comparative prevalence of tuberculous disease among homozygous and heterozygous twins and in various familial groups have made clear that hereditary factors condition the type of response to tubercle bacilli.

Evidence that an increase in resistance can occur through selection is provided by the change that occurred in the character of tuberculosis among the Plains Indians of the Qu'Appelle Valley reservation in Saskatchewan. Shortly after these Indians were first placed in the reservation late in the 19th century, the annual death rate from tuberculosis among them reached the fantastic figure of 900 per 10,000 population. More than half of their families were eliminated in the first three generations of the epidemic. During the first and second generations of the epidemic in the Qu'Appelle reservation, extensive glandular involvement was the rule in school age children. Meningitis, generalized miliary disease, bone and joint disease were extremely frequent — evidence of inability of the host to localize infection. In 1921, at a time when the generalized epidemic was in the third generation, the disease showed a greater tendency to localize in the lung and to exhibit a chronic course, the mortality was falling, glandular involvement had dropped to 7% among Indian school children. This latter manifestation of high susceptibility to the disease has continued to decline steadily and it affects now less than 1% of the Indian children in the present (fourth) generation.

What has happened to tuberculosis among the Qu'Appelle Valley Indians has happened or is happening among other Amerindians, the Polynesians, and the Eskimos. The same pattern also applies to the evolution of tuberculosis in our own communities. The history of family groups strongly suggests that this mechanism operated in Europe and America during the 19th century epidemics of tuberculosis, as it did certainly when the disease eliminated so many families among the Indians of the Qu'Appelle Valley reservation. One of the reasons why tuberculosis in the Western World of the 20th century presents a less acute character than it did in the past is that we are the fortunate beneficiaries of the tremendous selective process brought about by the widespread epidemics of a few generations ago.

Although so very incomplete, the knowledge of the factors that affect the evolution of microbial diseases has led to spectacular successes in their control. It is of importance, however, to look more closely into what is meant by the statement that microbial diseases have now been *conquered*, for this will make clear that many practical problems remain to be solved after the so-called "conquest". There is no doubt of course that the mortality due to infection is now at an all-time low. But it is also a fact that the amount of disease due to infection is still very large. Today, as in the past, microbial diseases account for the largest part of absenteeism from school, from gainful work, and from training in the armed forces; they remain the cause of an enormous amount of misery and a huge economic burden. To prevent death from infection has proved a far easier task than to ward off disease.

So far, the science of medical microbiology has been concerned chiefly with the acute disease processes caused by agents introduced from the outside. It is in this area that it has achieved its most spectacular successes — in diagnosis, prevention, and therapy. But the techniques developed to deal with acute infections have often proven wanting when applied to the immensely varied and ill-defined infectious ailments that constitute such a large percentage of medical practice. It is becoming increasingly apparent furthermore that most of microbial disease today is caused by agents which are ubiquitous in our communities and are harboured constantly by many normal individuals.

To understand the problem of infection as it occurs in its most prevalent form today, it is essential to realize that all human beings become at some time infected with a host of viruses, bacteria, fungi, and other microorganisms which are potentially pathogenic. In most cases, these infections remain latent or silent; a state of biological equilibrium is achieved between microbe and man as a result of various adaptive mechanisms. But equilibrium between microbe and man remains stable only under conditions similar to those under which the relationship has evolved, and it can be disturbed by any change in the internal or external environment of the infected individual. Thus in many cases, the effective determinant of a microbial disease in a given individual is not the event of infection, but rather any situation which upsets the equilibrium between host and parasite — whether it be a nutritional or an emotional disturbance, mental overwork, or a sudden change in weather.

The incidence of latent infections is likely to increase, since, as is well known, even the most successful chemotherapy usually fails to eradicate microorganisms from the body of the individual once infected. The continued existence of this enormous reservoir of microbial "persisters" provides the opportunity for the various stresses and

strains of life to evoke into activity latent infections that otherwise would remain dormant. An example which has become notorious during recent years is the prevalence of staphylococcal disease among patients receiving radiations or antifolic acid drugs for therapeutic purposes. In the past microbiological sciences have concerned themselves with the characteristics of microbial agents found in infectious processes. What needs to be investigated now are the factors responsible for converting dormant infection into disease.

Another aspect of the problem of infection which may become important in the modern world derives from the very effectiveness of public health measures. For example, German measles contracted in childhood entails little risk and gives a lasting immunity, but infection with the same virus can have serious consequences if first contracted during the early phase of pregnancy. Thus in this case, a hygienic way of life can convert a mild childhood disease into a serious disease of adulthood. Similarly, there is evidence that the increase in paralytic poliomyelitis in our population is due in part at least to the fact that viral infection is no longer contracted during the very first months of life as used to be the case in the past. The infected infant was then protected by the maternal antibodies, but these are no longer available when infection is delayed, as is so frequently the case today in the Western World. Thus, effective plumbing may have contributed to the increase in paralytic poliomyelitis among adults. These two examples illustrate the possibility that by controlling too efficiently the mild diseases of early childhood, we are paving the way for diseases of adulthood that were formerly unknown or of little importance.

With much hesitation, I shall now venture to formulate a few speculative thoughts concerning other possible consequences of present-day medical philosophy. In the past, many more children were born than survived and than were needed to maintain the population level. Now medical science permits, and ethics demand, that all children survive, however defective they may be physically or mentally. This progress, so great from the humanitarian point of view, is unfortunately fraught with unforeseeable social and biological consequences. Many individuals who would have died young without leaving any progeny now survive and reproduce because they are provided with continued and expensive medical care. There is no way to predict the distant outcome of this state of affairs because it has no precedent in the life of man. At the most one may suspect that the biologically defective will become an increasingly heavy burden for society, and one may wonder to what extent the accumulation of genes associated with hereditary disorders will alter significantly the constitution of the human stock.

It is worth asking, for example, whether the virtual eradication of tuberculosis—especially dur-

ing the years of childbearing—may not eventually result in back mutations and return the population as a whole to a state of susceptibility comparable to that of the Polynesians, Amerindians and Eskimos before they had come into widespread contact with the disease. Since tuberculosis epidemics appear to have cycles of approximately 100 years, a genetic loss of innate resistance would probably require at least three generations before becoming manifest, and therefore the danger need not worry us at the present time. But the problem is of sufficient biological interest and practical import for the future, to demand vigilance and pointed studies.

I realize, of course, that in the case of man, biological fitness must be defined in terms of the social environment in which he lives, and of the function that he performs in the group. By controlling the environment, and with the help of modern medical resources, man can live and function effectively in the modern world even though he be tuberculous, blind, diabetic, crippled, or psychopathic. But fitness to a complex society has economic implications that have not yet been precisely determined. There is no doubt that medical science increases the percentage of individuals unable to pull their full weight, and we may assume that this trend will continue at an accelerated rate, precisely by reason of medical progress. It is apparent also that the cost of medical care will continue to increase because each new discovery calls into use more specialized skills and costly items. In a recent report it was revealed that one million American families spent 50% of their total familial income on medical care during 1952, and 8 million were in debt on that account!

Moreover, and contrary to common belief, medical services are not self-limiting. It was thought at one time that by making proper therapy and public health procedures available to all, disease could be banished from society and thus medical costs decreased. In reality, however, new medical problems continuously emerge—some arising as modified forms of the old ones, others being created by social and technological changes. There must be some upper limit to the percentage of national income that can be spent on medical care, and a time may come when social and medical ethics will have to be reconsidered in the harsh light of economic necessities.

Clearly, we must not and we will not renounce our humanitarian and religious ideals. We will continue to regard all life as sacred, and worth preserving whatever the cost. No human being worthy of his salt would deny medical aid for the unfit and succour for those in distress. But we must be aware of the fact that the human values and techniques recently introduced into the biological arena create new problems that will have to be met by subsequent generations. It is not likely that these problems can be solved merely by

applying the knowledge developed under former circumstances.

I find it difficult to conclude this presentation by a simple summary because the facts that I have discussed encompass two contrasting aspects of the evolution of microbial diseases. It is true that we have gone very far toward controlling some of the acute killing infections that prevailed in the past. But it is folly to speak of *the conquest of disease*. Health is an expression of perfect fitness to the environment. As man and his environment change continuously, fitness is never permanent, disease will continue to occur, and unfortunately the cost of its control will continue to increase. Utopias are dreams that never come to pass.

Since I cannot thank here all those to whom I owe an intellectual debt,\* allow me to end by quoting what the English epidemiologist, William Farr, wrote in one of his annual letters to the Registrar General: "The infectious diseases replace each other, and when one is rooted out it is apt to be replaced by others which ravage the human race indifferently whenever the conditions of healthy life are wanting. They have this property in common with weeds and other forms of life, as one species recedes another advances." No comparison could be more apt. However well tended the garden, weeds and insect enemies constantly threaten the crops. Like gardeners whose work never ends, students of disease must always be on the lookout for new problems of infection. The control of microbial diseases is a never ending task that demands eternal vigilance.

#### RÉSUMÉ

Les maladies elles-mêmes ont très peu changé depuis les temps préhistoriques, cependant leur fréquence et leur gravité ont varié d'une génération et d'un genre de civilisation à l'autre, ce qui laisse supposer que l'expérience du passé ne servira pas nécessairement à résoudre les problèmes de l'avenir. Ces fluctuations avaient déjà été notées par Fracastor à l'égard de la syphilis. Nicolle devait plus tard parler de la "Naissance, vie et mort des maladies infectieuses". La disparition spontanée de la lèpre au XVI<sup>e</sup> siècle ainsi que de la suette anglaise à l'époque des Tudor illustre ce fait.

En 1701, la fièvre scarlatine n'était guère plus qu'un nom dans les annales de la médecine. En 1801, cependant, Graves rapporte qu'elle a causé de grands ravages à Dublin; trois ans plus tard, elle a perdu de sa virulence et de son importance. En 1840, cependant, la mortalité causée par la fièvre scarlatine a subitement doublé en Angleterre et au Pays de Galles et la courbe atteint un sommet en 1863. Cette intensité se perdit de nouveau à la fin du siècle dernier.

L'histoire de la rougeole offre des vicissitudes semblables. En 1785, Heberden affirme que la rougeole présente très peu de danger et qu'il est rare qu'on consulte un médecin pour cette indisposition. Cependant un virement soudain se produisit en 1800 si bien qu'en 1808 la mortalité de la rougeole dépassa celle de la petite vérole et son intensité à cette époque sembla comparable à celle de la rougeole maligne décrite par Sydenham en 1674. Après avoir été la première cause de mortalité infantile jusqu'en 1840, elle céda le pas à la scrofule jusqu'en 1915 où elle subit une recrudescence pour ensuite décliner jusqu'à nos jours.

La tuberculose, fléau des jeunes adultes, a diminué dans la seconde moitié du XX<sup>e</sup> siècle bien avant que la vaccinâ-

tion ou la chimiothérapie aient pu exercer quelque influence sur le cours de son évolution.

L'introduction de maladies microbiennes chez les populations vierges (Polynésiens, Africains, Esquimaux) cause des ravages inouïs. Pour s'en persuader on n'a qu'à se reporter aux effets catastrophiques de la rougeole, de la coqueluche et de l'influenza à Hawaï en 1848.

Les modalités historiques de notre conception actuelle de l'évolution des maladies infectieuses portent l'empreinte de trois grands noms de l'histoire de la science. L'effet que produisent de nouvelles entités morbides chez des populations qui auparavant n'avaient jamais été exposées à ces maladies, montre la valeur du principe de l'isolement géographique de Darwin. C'est à l'étude de la fièvre récurrente en Silésie que Virchow se persuade de l'importance du milieu physique et social dans la résistance à la contagion. Enfin, l'apport de Pasteur à l'étude des maladies contagieuses se passe de commentaires. En dépit de ces contributions les facteurs qui jouent dans les variations du comportement animal et de la susceptibilité à l'infection demeurent encore inconnus. La croyance populaire que la guerre, la famine et la peste chevauchent ensemble indique qu'on avait déjà remarqué que le niveau de vie et l'état de nutrition en particulier affectent profondément la résistance de l'homme à ces pathogènes en puissance. On sait depuis Pasteur que les microbes peuvent subir des altérations génétiques qui modifient leur pathogénicité; ainsi, de nouvelles épidémies peuvent transformer dans un sens ou dans l'autre la virulence du germe qu'elles propagent. Le contact antérieur avec l'agent infectieux confère à l'individu une augmentation de résistance à l'infection: plusieurs petites doses infectieuses peuvent produire une immunité humorale ou cellulaire. Les changements génétiques qui se produisent au sein des populations exposées aux épidémies se prêtent difficilement à une étude biologique précise. Il est cependant raisonnable de présumer que les survivants d'une épidémie où la mortalité est très élevée doivent posséder dans leurs gènes une certaine résistance qui a permis leur survie. La résistance progressive des Indiens de la vallée Qu'Appelle à la tuberculose depuis la fin du XIX<sup>e</sup> siècle en fournit un exemple.

En dépit de notre connaissance incomplète des facteurs qui affectent l'évolution des maladies microbiennes l'application de nos connaissances à leur contrôle a produit des succès spectaculaires. Si la mortalité causée par ces maladies est plus basse qu'elle ne l'a jamais été, il est bon de se rappeler avant de parler de leur "conquête", que la morbidité causée par l'infection est encore très vaste.

On ne possède une conception satisfaisante du problème de l'infection qu'en se rappelant que l'être humain à un moment ou l'autre de sa vie est infecté par un grand nombre de virus, de bactéries, de champignons et d'autres micro-organismes, tous en puissance de développement. La plupart du temps ces infections demeurent latentes ou silencieuses alors que s'établit un équilibre biologique entre le microbe et l'homme. Toute influence du milieu interne ou externe qui tend à rompre cet équilibre peut donner naissance à l'infection. Les recherches médicales devraient à l'avenir se porter sur les facteurs responsables de la transition entre une infection latente et une maladie déclarée.

Il n'est pas inutile de souligner ici que l'efficacité des mesures d'hygiène publique est une arme à deux tranchants. L'éradication de la roséole épidémique dans l'enfance a fait de cette maladie essentiellement bénigne la cause d'anomalies congénitales chez les enfants des femmes qui l'ont contractée au début de la grossesse. De même peut-on rattacher l'augmentation de la paralysie chez les adultes atteints de polyomélite à une amélioration dans les canalisations d'eau potable et dans la disposition des eaux-vannes.

La proportion des nouveau-nés qui atteignent l'âge adulte est plus forte de nos jours qu'elle ne l'a jamais été. Ce progrès humanitaire peut avoir des conséquences sociales et biologiques de grande envergure. La survie des biologiquement faibles peut devenir un lourd fardeau pour la société et l'accumulation des gènes associés aux troubles héréditaires n'arrivera-t-elle pas à adultérer la race humaine?

La santé biologique de l'être humain doit être définie en fonction du milieu social où il vit et du rôle qu'il joue dans la communauté. Le contrôle du milieu peut lui permettre d'évoluer d'une façon satisfaisante même s'il est tuberculeux, aveugle, diabétique, paralysé ou psychopathe. Ce contrôle et le progrès des sciences médicales qui permet cette adaptation sont en voie de devenir très coûteux. Peut-être atteindrons-nous un jour la limite du pourcentage du revenu national qu'il est économiquement possible de

\*For this reason, I do not append a bibliography that would be far too long.

consacrer aux soins médicaux sans grever au delà de leurs limites les ressources de la société et alors serons-nous forcés de reviser notre éthique sociale et médicale à la lueur des nécessités économiques. Il n'est pas question de renoncer à notre idéal humanitaire et religieux, mais il faut reconnaître que ces problèmes ne pourront pas être résolus par l'application de connaissances acquises dans le passé,

L'auteur termine en citant l'épidémiologiste William Farr, qui écrivait jadis: "Les maladies infectieuses se succèdent et quand l'une est extirpée une autre la remplace, ravageant la race humaine de façon indifférente lorsque les conditions propices à la santé font défaut. Elles ont ceci de commun avec les mauvaises herbes et les autres formes de vie que lorsqu'une espèce décline une autre en profite".

## THE UVEO-ENCEPHALITIC SYNDROME OR VOGT-KOYANAGI-HARADA DISEASE

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THIS RELATIVELY RARE DISEASE is characterized by the unusual combination of uveitis, depigmentation of skin and hair, and cerebral manifestations. It has long been recognized by ophthalmologists, and reports of cases have been confined almost exclusively to the ophthalmic literature. But it may present a diagnostic problem to general physicians, neurologists, neurosurgeons, and dermatologists. We propose to review the literature, to report five more cases and to discuss the etiology of the condition. We hope that the publication of this review in a general medical journal may help to spread the knowledge of this disease beyond the ophthalmological domain.

### REVIEW OF THE LITERATURE

Like so many other conditions it was first described by Jonathan Hutchinson<sup>1</sup> in 1892, although Vogt<sup>2</sup> is usually given the credit for being the first to do so in 1906. Other single cases were then reported in the literature, particularly in Japan, where it appears to be more common.

In 1929 Koyanagi<sup>3</sup> wrote the first significant account of the disease. He reviewed the literature and 16 cases, 12 of which were collected from case reports and 4 of his own. He described the clinical picture of headache, fever, bilateral uveitis, dysacusia, vitiligo, poliosis and alopecia. He emphasized that the uveitis was essentially anterior in situation but did mention that exudative retinal detachment occasionally occurred. Following Koy-

anagi's publication this condition was known as the Vogt-Koyanagi disease.

In 1926 Harada<sup>4</sup> described five cases characterized by bilateral posterior uveitis with inferior exudative retinal detachments.

For nearly two decades it was considered that the Vogt-Koyanagi disease and Harada's disease were two separate entities, the difference being that in the former the uveitis was anterior in situation and no detachment occurred, whilst in the latter condition the uveitis was posterior and was accompanied by retinal detachment. But this distinction is not justified. Koyanagi<sup>3</sup> mentioned that retinal detachment occurred in two of his cases, and in a typical case of Vogt-Koyanagi disease the anterior uveitis is so severe that a retinal detachment is likely to be obscured and missed. Harada<sup>4</sup> mentioned in his article that severe anterior uveitis may occur and recorded that one of his cases had severe alopecia followed by the growth of fine white hair.

Many cases have now been described and it is generally agreed<sup>5</sup> that the Vogt-Koyanagi disease and Harada's disease are identical, but that the severity of the manifestations in different sites may vary from case to case and produce marked differences in the clinical picture. There is now a tendency to drop the eponymous title and to give the condition a name indicating the nature of the disease. Yuge<sup>6</sup> has suggested the title of oculo-cutaneous syndrome, but this fails to indicate the meningitic features. Cowper<sup>7</sup> first suggested the name uveo-encephalitis. We feel that this is perhaps the most explanatory term for this bizarre condition. The integumentary changes tend to occur late and, though significant, diagnostically they are less dramatic than the early cerebral features and the uveitis.

### CLINICAL FEATURES

Great variations in the severity of the clinical picture may occur and incomplete manifestations of the disease are probably common. Walsh<sup>8</sup> pointed out that bilateral uveitis with pleocytosis of the cerebrospinal fluid is not uncommon and that such cases should probably be considered as "formes frustes" of this disease.

Cowper<sup>7</sup> suggested that the clinical course of the disease usually falls into three phases: (1) meningeal phase; (2) ophthalmic phase; (3) convalescent period.

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1. *The meningeal phase* usually begins with an abrupt onset and lasts from two to four weeks, with low fever which may be persistent, and retro-ocular or frontal headache causing insomnia and irritability.

2. *The ophthalmic phase* may follow the meningeal phase but occasionally they occur simultaneously. Both eyes are affected and the patient complains of photophobia, tearing and rapid loss of vision. Inflammatory cells appear in the aqueous and vitreous, so that the media are hazy and funduscopic examination may be difficult or impossible. The anterior part of the uveal coat may be chiefly affected so that the condition presents as iridocyclitis. When the posterior uvea is involved, the optic discs and the retinal veins may be swollen, resembling papilloedema or papillitis. Harada<sup>4</sup> emphasized the appearance of gross oedema of the retina, so that the optic disc seemed to be at the bottom of a funnel. Retinal haemorrhages may occur.

A gradual sinking of the fluid exudate results in bilateral inferior retinal detachments, which may be slight and peripheral or so gross that the macular area is involved. The medial haze may be so severe that it is impossible to see the retinal detachments with an ophthalmoscope. However, their presence may be indicated by an absence of the sense of light projection in the upper visual field. This occurred in Case 3.

No particular visual field defect is characteristic of this condition. General contraction, enlargement of the blind spots and central scotomata have all been reported.

Headache, vomiting, neck rigidity and a positive Kernig sign may be present. Deafness with or without tinnitus may cause the patient much concern. It is usually bilateral but tends to disappear in several weeks. The cerebrospinal fluid may show marked pleocytosis and increased pressure.

At this stage the clinical picture may resemble that of a rapidly expanding intracranial lesion so closely that several cases have been reported in which exploratory craniotomies were performed. Our third case was so treated.

The ophthalmic phase lasts from three to five months.

3. *Finally, the convalescent period follows*, and it may last from six to twelve months. The sub-retinal fluid absorbs slowly and the retina becomes reattached. Scattered white exudates often persist for some time in the previously detached area, but they gradually absorb and disappear. The fundi become depigmented so that the choroid is more obvious than normal. Strands of fibrosis and patches of pigmentation may be grouped about the optic disc. Less than 30% of patients regain useful vision because secondary glaucoma, cataracts, optic atrophy and phthisis bulbi may occur. The ectodermal manifestations of poliosis, vitiligo

and alopecia may appear during this period and are usually permanent.

#### CASE REPORTS

**CASE 1.**—Mrs. H.L., aged 34 (one parent was Italian), had a brief attack of iritis in the right eye in December 1952. The inflammation subsided in two or three days following an injection of typhoid vaccine. No investigations were carried out at this time.

She was first seen on April 24, 1953, when she complained that for two weeks she had suffered a severe continuous periorbital ache which was worse at night and was not relieved by aspirin. During this time the vision of the left eye had been blurred. Five days previously a black spot suddenly appeared before the right eye. On examination, with a plus 2.00 D sphere correction before each eye, vision was reduced to Rt. 20/100 and L. 20/200. She had bilateral iridocyclitis and marked macular oedema. A central scotoma was present in each eye (Fig. 1).

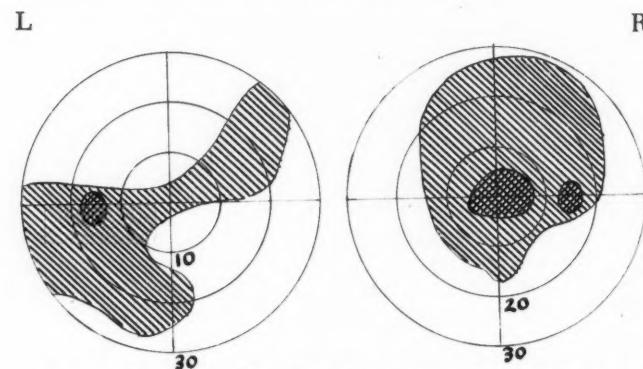


Fig. 1.—April 24, 1953. Targets 3/1000 white, 5/1000 white.

A general medical examination revealed no defect. Radiographs of the teeth, sinuses and chest were normal. Blood examination and urinalysis revealed no abnormality. An audiogram revealed no hearing loss. A Mantoux test was negative.

She was treated with atropine eyedrops and the corrected vision gradually improved to 20/30 and 20/50 by May 19, 1953.

After one month's observation, i.e. six weeks after the onset of the disease, alopecia areata of the scalp and poliosis of the eyelashes first appeared. By this time the ocular inflammation had almost completely subsided. Examination with the binocular microscope revealed no keratic precipitates but slight endothelial bedewing was still present.

After a period of nine weeks, the inflammation had completely subsided, and her vision had improved to 20/30 in each eye despite minimal paramacular scotomata (Fig. 2).

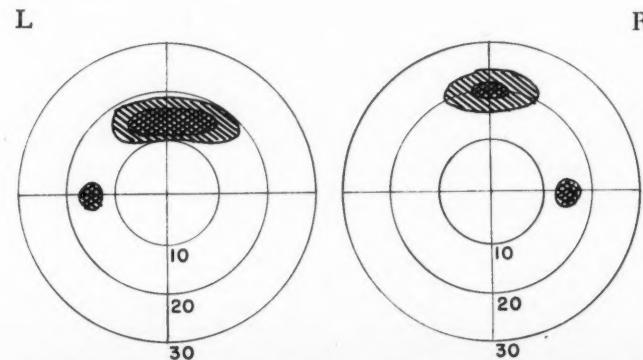


Fig. 2.—May 12, 1953. Targets 3/1000 white, 5/1000 white.

CASE 2.—J.S., a 29-year-old Hungarian immigrant with a previous history of good health, was admitted to the neurological service of the Toronto Western Hospital on January 25, 1956, complaining of headache, fever, sore throat and diarrhoea, of five days' duration. In the two months before admission he had been working with animals in a laboratory, including monkeys used for preparing Salk vaccine. In November and December 1955, he had received 15 c.c. of gamma globulin and had been immunized with three injections of Salk vaccine.

On admission he was drowsy and flushed, with a rectal temperature of 105° F. He had a moderately injected pharynx but no other positive findings except for a questionable left facial weakness. The fundi were reported to be normal and venous pulsation was present at each optic disc.

During the first week in hospital his temperature gradually fell although he received no specific therapy. His mental state fluctuated from lethargy and drowsiness to apprehension. He complained of intermittent headache, and cerebration was slow. There were occasional brief shivering spells. On the fifth day he began excreting about 10,000 c.c. of urine of low specific gravity per day. A diagnosis of diabetes insipidus was made and this condition was controlled by intramuscular injections of Pitressin tannate in oil, 1 c.c. daily.

An electroencephalogram revealed a poorly organized alpha rhythm and many runs of 4-7 cycle per second activity in random fashion from all areas. There were also runs of bilaterally synchronous short bursts of 3 cycle per second of high voltage from all areas. This suggested a diffuse brain disorder which included the deep central structures.

In the second week, though he was now afebrile, his mental state deteriorated. He was alternately drowsy and restless, and occasionally confused and very resistive. Delirium and hallucinations developed. Speech became slurred and his movements incoordinated, especially of his left arm. Left facial weakness and left hemiparesis became evident.

The visual acuity could not be tested because of the confused mental state. The pupils were fixed and dilated. The fundi were pale and, in the mid-periphery, patches of white exudate were seen along the course of the nasal branches of the central retinal arteries. In places the arteries could not be seen and several streaky haemorrhages were noticed with the exudates. The arteries were extremely spastic. A moderate amount of oedema was present around the right disc, but it was not elevated and venous pulsation could be seen. A clear view of the fundus was not possible because of vitreous haze.

Between the second and fifth week the patient's mental state improved. His left hemiparesis exhibited peculiar fluctuations in severity with occasional improvement followed by exacerbation of weakness. There was also a variable intensity of true cerebellar ataxia of the left arm. His mental state gradually improved and he became cheerful and talkative with brief episodes of confusion, aggression and automatism. These latter periods seemed to coincide with recurrence of the left-sided weakness and clumsiness. The diabetes insipidus worsened, necessitating larger amounts of Pitressin. By this time the retinal oedema had cleared and the white patchy exudates with the superficial haemorrhages were more distinctly outlined.

In his sixth week the patient complained of deteriorating vision. Re-examination showed a visual acuity of 20/60, .60 M print in the right eye and 20/80 .75 M print in the left. The vitreous haze had increased and large white precipitates indicative of uveal inflammation were noted on the corneal endothelium, although no flare or cells were seen in the anterior chamber.

By the eighth week, vision in the right eye was reduced to hand movements at three feet (90 cm.) and a large bullous retinal detachment was seen in the lower half of the fundus. Vision in the left eye was 20/70 and no detachment was seen. Frequent examinations failed to reveal a retinal hole. Because the patient stated that his vision was better after a night's sleep, he was kept at complete bed rest with both eyes occluded for a week. This failed to improve his visual field and the fundal appearance did not alter. At this point, two months after admission, no neurological abnormality, apart from the eye signs and the diabetes insipidus, could be elicited.

He was then given oral cortisone, 300 mg. daily. This dosage was reduced gradually over a three-week period. No change occurred in the ocular findings but the diabetes insipidus required more Pitressin for control.

Between the ninth and sixteenth weeks the vitreous haze gradually cleared in both eyes, and extensive thin grey retinal deposits associated with the retinal arteries in the mid-periphery could be seen. The patient's vision in the right eye improved to counting fingers at two feet (60 cm.) but deteriorated to 20/100 in the left eye. He complained of seeing a series of fine black circles surrounding patches of red and green spots on opening his right eye.

Five months after the patient's admission he developed a frankly psychotic mental reaction, depressive and paranoid in type, and was admitted to a provincial mental hospital where he has remained.

One year after the onset of his illness the patient was quiet, withdrawn and delusional, but co-operative. The diabetes insipidus required only intermittent injections of Pitressin for control. The visual acuity of each eye and the appearance of the anterior segments remained unchanged. The vitreous opacities and grey retinal deposits were still present in both eyes, and the detachment in the right eye was complete. In the left eye the retinal arteries were attenuated and the upper nasal branch appeared occluded and sheathed near the optic disc. Areas of choroidoretinal atrophy were seen but pigment cell proliferation was not a noticeable feature. The disease was apparently inactive, and the prognosis for mental and visual improvement seemed poor.

The white cell count and differential were normal on admission but the blood smear showed several large atypical lymphocytes. The erythrocyte sedimentation rate, serum protein, and electrolyte values were normal. Blood and spinal fluid Wassermann tests were repeatedly negative, but the treponema immobilization test was positive on two occasions. It was also of interest that the spinal fluid demonstrated a colloidal gold reaction of 5554331000 three weeks after admission, while one month later this reaction was 0123210000. No history of luetic infection was obtained. Intradermal skin testing was positive with 1/20 mg. of old tuberculin and negative with toxoplasmosis antigen.

The initial spinal fluid cell count was 188 per c.mm., consisting chiefly of lymphocytes, and it gradually fell to normal one month later. Spinal fluid protein was 40 mg. % on admission and rose to 56 mg. % three weeks later before returning to normal. Cultures of the throat, blood, stool, urine and spinal fluid did not reveal significant pathogens. Complement fixation reactions to *Listeria* antigen were positive but the results indicated a past infection. Extensive virus studies on the spinal fluid in the acute phase, using tissue culture techniques and a variety of experimental animals, failed to reveal any pathogens. The patient's serum was submitted to neutralization tests against 26 different virus strains previously isolated from various cases of encephalitis. In no instance was this informative.

Three months after admission 0.5 c.c. of sub-retinal fluid was removed from the patient's right eye. A small amount was injected into the aqueous of one eye and into the vitreous of the second eye of a rabbit. Two weeks later the eye which had received the vitreous injection had a moderately severe uveitis with a flare and cells in the anterior chamber. The vitreous and aqueous of this eye were passed into tissue culture and into the eyes of a second rabbit but no further activity developed.

**CASE 3.**—This Chinese patient was born in Canton in 1897 and emigrated to Canada in 1910.

On February 5, 1954, he was admitted to hospital for investigation. He had had a severe headache for ten days and progressive loss of vision for seven days. The pain was situated just behind the eyes. There was no dizziness, vomiting or any other significant symptom.

General physical examination revealed no abnormality although he had a low-grade fever at this time which reached 100° F. on one occasion. His vision was reduced to perception of light. There was marked conjunctival injection. Early lens opacities and vitreous haze rendered fundus details difficult to see but the optic discs could be seen to be oedematous and there was some congestion of the retinal veins.

At this stage urinalysis, radiographs of skull and sinuses, and blood Kahn reaction were reported negative. Blood examination showed a polymorphonuclear leukocytosis of 17,000 and a sedimentation rate of 26 mm. in one hour. On lumbar puncture the cerebrospinal fluid pressure was found to be 18 cm. water. The cerebrospinal fluid colloidal gold curve and Wassermann and Kahn reactions were negative but lymphocytes were 450 c.mm. and protein value was raised to 59 mg. %. The result of a glucose tolerance test was normal.

A space occupying lesion in the frontal region was suspected and the opinions of a neurosurgeon and an ophthalmologist were obtained. Bilateral central scotomata were present, and both considered the condition to be bilateral optic neuritis. He was treated with 500,000 units penicillin twice daily from February 14 to February 21, and cortisone was given in addition from February 19 to 21, the dose being 50 mg. 4 times a day.

At this time his headaches had reduced in severity but there was no improvement in vision.

He then went to Montreal, and was admitted to the Montreal Neurological Institute on February 22, 1954.\*

At the time of this admission he had slight headaches in the evening and morning. His vision was reduced to light perception and hand movements in the inferior part of the field of each eye. In each eye were early lenticular opacities and some congestion of the retinal veins.

Examinations of the urine on February 24 and February 26 showed traces of sugar. A lumbar puncture on February 23, 1954, revealed a normal pressure, protein 35 mg. % (Pandy negative), sugar 75 mg. %, chlorides 748 mg. %, Lange 001111000, Wassermann negative, and 650 cells per c.mm., mostly lymphocytes and a number of large mononucleated cells thought to be neoplastic.

On February 23, the blood examination showed haemoglobin value 96%, erythrocytes 4.8 million, leukocytes 12,200. The differential count was neutrophils 77%, lymphocytes 19%, monocytes 2%, eosinophils 2%; haematoctrit value 41, sedimentation rate 20; non-protein nitrogen (N.P.N.) 29.4 mg. %. The blood phosphatase and cholesterol were normal.

A radiograph of the skull on February 23, 1954, was reported to show diffuse decalcification of the bone around the left side of the sella turcica. There was no direct invasion of the bone and no evidence of paranasal sinus disease. This was considered to suggest a parasellar expanding lesion on the left side.

The following day a pneumoencephalogram was done. It was reported that the superior surface of the diaphragm of the sella turcica had not been visualized. This was taken to indicate that the diaphragm was either tilted, elevated or covered with some abnormal soft tissue mass.

On February 25, 1954, a left frontal craniotomy was performed and the chiasmatic cistern was explored. No evidence of neoplasm was found, but adhesions were present around the chiasm tending to bind the subcallosal region to the optic nerves. When the left optic sheath was incised there was no bulging of its contents.

The patient recovered from his operation without complications. Postoperatively he was given intensive penicillin therapy, of one million units a day for ten days, with no benefit. He was then given 150 mg. cortisone daily for nine days, later reduced to 75 mg. a day.

The glucose tolerance test results on March 3, 1954, were: fasting—112 mg. %, 1 hour—260 mg. %, 2 hours—224 mg. %, 3 hours—108 mg. %, 4 hours—92 mg. %, 5 hours—66 mg. %.

On March 15, 1954, another examination of the cerebrospinal fluid revealed no significant change except that the cells were reduced to 170 in number. Numerous cultures of the cerebrospinal fluid for bacteria and fungi were negative.

At the time of discharge, re-examination showed that the medial opacities had cleared surprisingly and that the retina was detached in the lower half of the left eye and probably in the right eye as well.

At his discharge from the Montreal Neurological Institute the diagnosis was considered to be bilateral lens opacities, optic neuritis of unknown etiology and inferior retinal detachment.

\*Dr. Wilder Penfield kindly supplied the report of the findings at the Montreal Neurological Institute, and the patient's medical history in Regina was provided by Dr. J. M. Ferries, Dr. Douglas T. Martin, Dr. P. B. Ryan and Dr. W. L. Kurtze.

He returned to Regina and was in hospital from March 28 to June 17, 1954. During this time he was treated with cortisone 25 mg. 4 times a day and ascorbic acid 50 mg. 3 times a day, and was given some injections of vitamin B<sub>12</sub> and sterile milk. At this time he could distinguish between light and dark.

On July 16, 1954, he was examined again and much scattered pigment could be seen in the lower half of each fundus resembling an old choroiditis.

On October 17, 1954, he was again admitted to hospital with bilateral acute glaucoma secondary to iris bombe. Bilateral iridectomy was performed, followed by treatment with atropine and cortisone. He was discharged on November 12, 1954. Iridocyclitis recurred on November 24, 1954, and it was treated with atropine, cortisone and injections of sterile milk.

The condition then remained quiescent. He was blind but had no return of acute symptoms.

He was referred to the Eye Department of the Winnipeg Clinic on January 23, 1956. On examination he was found to have a mature cataract in each eye with the iris adherent to its anterior surface. The iridectomy on each side was partially filled by organized exudate but there was no evidence of active inflammation. Light perception was present in each eye but the sense of light projection was inaccurate.

Patches of vitiligo were present on his back and both hands. He stated that these developed at the time of the onset of the disease in February 1954.

It was explained to him that whilst there was little hope of great recovery in vision, cataract extraction offered the only hope of any improvement. A left intracapsular extraction was performed on January 26, 1956, and a right intracapsular extraction on February 15, 1956. At each operation a piece of iris was removed for histological examination. He made a good recovery and was discharged on February 29, 1956.

Dr. D. W. Penner, pathologist to the Winnipeg General Hospital, reported on the histological appearance as follows:

"The iris is oedematous and shows migration of pigment. Scattered throughout is a rather dense infiltration of numerous plasma cells, almost an equal number of lymphocytes with an occasional large mononuclear cell and only very infrequent eosinophils. In one area there is a prominent proliferation of fibroblasts. These are young fibroblasts and in areas form a 'tubercle-like' grouping. No true epithelial or giant cells are seen. The picture is that of a non-specific chronic inflammatory reaction."

He was last seen on April 30, 1956. His vision was then perception of light with each eye, but the sense of light projection was not accurate in all quadrants of the field. The vitreous of each eye was still hazy, preventing a clear view of the fundus. Each optic disc was pale and the retinal arteries were narrow. No abnormal pigmentation or scarring of the fundi could be seen.

CASE 4.—Mrs. N.C., aged 29. This patient, who was part Indian, was first admitted to the University of Alberta Hospital to the service of Dr. R. W. Robertson in September 1953. Two months previously she had pain in the left eye with progressive impairment of vision. One week later, the right eye became similarly affected. The vision in the two eyes fluctuated with the pain in the eyes, the vision being worse when the pain was severe. Examination of the eyes showed

bilateral choroidoretinitis with haziness of the media. The visual acuity was right—20/20; left-hand movements at 2 feet.

*Laboratory findings.*—Kahn test negative; Hb. 10.5 g. %; R.B.C. 3.78 million; W.B.C. 12,700; neutrophils 82%; lymphocytes 17%; monocytes 1%; haematocrit 34%; sedimentation rate (corrected) 22 mm. in one hour; chest x-ray examination negative.

She was treated with 25 mg. ACTH in 1000 c.c. normal saline given intravenously daily for twelve days. Cortisone 0.5% eyedrops were instilled locally. Throughout the admission she ran an irregular low-grade fever up to 99.8° F. On discharge her vision had improved. She was then seen frequently as an outpatient by Dr. Robertson for recurrent pain and "redness" of the eyes. On March 15, 1955, she was readmitted to the University of Alberta Hospital with severe pain in the right eye developing three days after a severe cold. On admission she had multiple "cold sores" around her mouth and some on her tongue. Examination of the eyes showed irregular fixed pupils. Neither fundus could be seen because of haziness of the media.

Her temperature was 102.2° F. and gradually fell to normal. At discharge on April 8, 1955, her vision was R.—light perception only, and L.—hand movements.

The laboratory findings were similar to those of the previous admission.

She was treated with cortisone orally starting with 100 mg. a day and tailing off to 25 mg. in three weeks and hydrocortone 2.5% drops to the eyes 4 hourly. Nine intravenous injections of Piromen were given.

On April 19, 1955, she was readmitted with pain in the left eye. It was so severe that she was crying and vomiting. Examination revealed secondary glaucoma and uveitis. She was treated and her symptoms gradually subsided.

She was readmitted in January 1956, two months pregnant. Her previous four pregnancies had been associated with a flare-up of her eye condition with precipitation of secondary glaucoma. In view of this, a therapeutic abortion was carried out and followed by hysterectomy.

After hysterectomy, she began to complain of headache. The left occipital region was chiefly involved and the pain tended to spread to involve the left side of the head. Towards the end of 1957, she had repeated vomiting attacks with headaches and fever. This was accompanied by increasing weakness of the right arm and leg so that she required a cane to assist her walking. She had no further pain in the eyes.

She was readmitted to hospital in February 1958 for neurological investigation. At this time she was looking much older than her years. She had moderate greying of the hair and marked facial vitiligo. There was no oral ulceration. Between bouts of distress with headache, she was rather euphoric.

On examination there was some stiffness of the neck. Apart from the eye changes the cranial nerves were normal. She had a right hemiparesis with about a 50% reduction in power. The tendon reflexes on the right side were increased, and the right plantar reflex showed an extensor response.

During this admission a low-grade fever up to 100° F. occurred.

*Investigations.*—The laboratory findings again resembled those of the first admission.

The E.E.G. showed a very low amplitude record with excess generalized slow wave activity.

*Cerebrospinal fluid.*—Cells 280; lymphocytes 90%; protein 70.4 mg. %; chlorides 734 mg. %; glucose 40 mg. %; colloidal gold 011000000; Pandy negative; Kahn negative.

This patient was most anxious to go to her children and was allowed out on the understanding she would return in ten days.

She was readmitted March 1958 and given Meticorten 40 mg. daily. After two weeks of therapy, her hemiparesis improved considerably. Her headache subsided and she was able to walk about without a cane.

**CASE 5.**—Mrs. G.B., aged 22, who is partially of Indian extraction, was first seen on December 13, 1957, complaining of transient double vision and pain and blurring of vision in the right eye. Ophthalmological examination at that time did not reveal any abnormality. Her visual acuity was 20/20 in each eye.

The following day she returned complaining of more pain and reduced vision in the right eye. On examination at this time the visual acuity was 20/50 in the right eye, and she had a central scotoma extending to 10°.

Her sight became progressively worse and by December 19 had deteriorated to R. 20/200, L. 20/100. She was admitted to hospital for investigation with a tentative diagnosis of bilateral retrobulbar neuritis. Pertinent findings at this time were: blood count: W.B.C. 7500, 67% neutrophils, 26% lymphocytes, 7% monocytes, Hb. 14.2 g. %, sedimentation rate 15 mm. in one hr. Cerebrospinal fluid cell count: 20 lymphocytes, 40 erythrocytes; glucose 70 mg. %.

The patient was given Meticorten 20 mg. twice a day and, although her visual acuity did not improve, she discharged herself on December 24, 1957.

The patient was readmitted to hospital on December 27, 1957. At this time her visual acuity was R. 18/200, L. 14/200. She complained of severe headache and severe pain in each eye. The optic disc margins of each eye were blurred. There was diffuse oedema throughout the entire retina of each eye, more concentrated in the macular region. This oedema gave the retina a striated clock dial appearance.

At this time the superficial and deep reflexes were found to be markedly diminished. Meticorten was again administered, and ACTH was given in addition.

December 28, 1957: A retinal detachment was present in the superior temporal and inferior temporal quadrants of the right eye. In the left eye there was an inferotemporal retinal detachment. The cerebrospinal fluid on this date contained 500 lymphocytes, glucose 50 mg. %, chlorides 742 mg. %, and protein 104 mg. %.

Acetazolamide (Diamox) 1000 mg. was given daily from December 28 to January 3, 1958.

December 29, 1957: In each eye the retinal detachment had increased and there was a corresponding decrease in the oedema at the posterior pole.

January 3, 1958: The cerebrospinal fluid cell count was 226 lymphocytes and sugar was 83 mg. %.

January 5, 1958: The retinal detachments had improved and were present in the temporal regions of each eye only. The remainder of the fundus revealed a peculiar fine pigmentation with scattered round circumscribed whitish-yellow dots.

The retinal detachments gradually subsided and on January 17, the patient was discharged from hospital.

The visual acuity had improved to R. 20/20 and L. 20/60. On slit lamp examination there was no flare in the anterior chamber of each eye. Early lenticular opacities were noted in each eye following the embryonal nuclear suture line. The posterior lenticular space and anterior vitreous was filled with fine pigment particles. On ophthalmoscopic examination the entire fundus of each eye had heavy pigment deposits, more concentrated in each macular region, and dispersed amidst these pigment deposits were peculiar round yellowish-white spots. The intraocular tension of each eye was normal.

She was next seen on April 25, 1958. By this time poliosis of the hair of the head had developed.

Intraocular and intraperitoneal injection of the patient's cerebrospinal fluid into rabbits was unsuccessful in reproducing this disease.

#### DISCUSSION

These five cases show the great variations in severity and clinical picture which may be encountered.

The first patient exhibited mild manifestations of the disease. Apart from the marked macular oedema, there were no posterior ocular manifestations of inflammation and iridocyclitis was not severe. The alopecia and poliosis developed six weeks after the onset of the disease. It is possible that a low-grade uveitis was present during the interval of four months after the first attack of iritis.

Case 2 developed the retinal detachment in one eye only and the detachment persisted. The case was unusual in that he developed a severe encephalitis which resulted in diabetes insipidus and a permanent psychosis. It might be argued that the psychosis was due not to the encephalitis but to the psychic trauma of the prolonged illness. The pigmentary changes in skin and hair did not occur in this patient.

The third patient had a condition typical of the picture described by Harada with bilateral retinal detachments. He had some features of the Vogt-Koyanagi pattern, however, because he later developed severe iridocyclitis with secondary glaucoma and cataracts. He became blind. This patient was thought to have a rapidly increasing intracranial space-occupying lesion, and an exploratory craniotomy was performed.

The fourth patient illustrates an unusual mode of onset because recurrent uveitis preceded the neurological signs. It is interesting that whereas the ocular manifestations failed to respond to corticosteroids, the neurological lesions rapidly responded to a dose of Meticorten which was more than double the previous dose. It might be argued that recurrent attacks of uveitis and secondary glaucoma, with on one occasion ulcers of tongue and mouth, are more in favour of a diagnosis of Behcet's syndrome. But there were no genital ulcers, no lesions were present on the legs, and the oral ulcers never recurred. Moreover, marked

vitiligo appeared on the face, and vitiligo is not a feature of Behcet's syndrome.

Case 5 presented as a bilateral retrobulbar neuritis and then developed into an apparently typical Harada pattern with good recovery.

#### ETIOLOGY

Two theories concerning the cause of this disease have been advanced, namely, that it is (a) a virus infection and (b) an allergy to uveal pigment.

The histological appearance of the uveal tract is that of a non-specific chronic granulomatous inflammation, and it does not especially favour either a virus or an allergy as the cause of this condition. At the present time the weight of evidence suggests a virus as being the cause, but it is by no means proven.

#### A. The Evidence Concerning the Viral Theory

The subretinal fluid of a case with detachment of both retinæ was inoculated into the vitreous of a rabbit by Tagami.<sup>9</sup> This resulted in a disease closely resembling the human condition. Takahashi<sup>10</sup> also injected vitreous from affected eyes into the basal cisterns of rabbits and produced a descending optic neuritis and uveitis. He then injected some of the brain tissue from an infected rabbit into the basal cistern of another and caused the same disease. Similarly optic neuritis and uveitis resulted when Malbran and Muhlmann injected vitreous from an eye with Harada's disease into the subarachnoid space of rabbits. Sugiura, Fukuda and Eda<sup>12</sup> inoculated mouse brain with material from eight eyes affected with uveo-encephalitis and two with sympathetic ophthalmia. Only from the eighth case of uveo-encephalitis, which happened to be an early one, was a virus grown. This was found to be neutralized by the blood serum of one of the other patients in a dilution of 1 in 100.

These findings suggest a viral origin, but Bruno and McPherson<sup>13</sup> injected the subretinal fluid of their cases into the brains of mice and were unable to confirm the results of the Japanese workers. Repeated egg embryo and mouse brain inoculations of aqueous, subretinal fluid and spinal fluid from affected patients at the Wilmer Institute<sup>14</sup> have also been negative. In our series subretinal fluid from Case 2 and cerebrospinal fluid from Case 5 were inoculated into rabbits' eyes but no virus was grown in either case. Moreover, as Walsh<sup>8</sup> has pointed out, the virus D disease is widespread in rabbits and it is possible that it may remain latent and be provoked into activity by an intracranial injection.

The results of the search for a virus are thus equivocal. But it must be remembered that the diagnosis is seldom made in the early stages. The negative reports in the literature may be due to the fact that by the time the diagnosis is made the

virus has disappeared. It may well be that a positive virus culture may be obtained if the aqueous, subretinal fluid or vitreous is inoculated at an early stage before the virus has disappeared from the ocular fluids.

The integumentary changes are difficult to explain. They develop about the third month in the course of the disease in at least 80% of cases. No satisfactory explanation of the alopecia, vitiligo, and poliosis in this condition has yet been advanced. It is still more difficult to relate these ectodermal manifestations to the uveo-encephalitis.

In his exhaustive study of this condition, Hague<sup>15</sup> reviewed the embryology and anatomy of the hypothalamic region and suggested that a lesion in this area might be responsible for the complaints of chilliness, the deafness, and the depigmentation. He quoted a patient of Vonderahe and Abrams<sup>16</sup> who had an ependymoma of the third ventricle and depigmentation of skin, alopecia, greying of the hair and polyuria. It is interesting that our second patient had diabetes insipidus but no depigmentation. Our third patient had some abnormalities of glucose metabolism and operation revealed adhesions in the hypothalamic area. Hague<sup>15</sup> pointed out that these observations might also be related to some of the unusual features of the Laurence-Moon-Biedl syndrome. It seems reasonable, therefore, to postulate that this condition might be due to a virus infection involving the hypothalamic area of the brain and the uveal tract of the eyes.

#### Relation to Sympathetic Ophthalmia

Harada<sup>4</sup> drew attention to the many ways in which the disease he described resembled sympathetic ophthalmia. The important difference between the two diseases is that sympathetic ophthalmia follows a penetrating wound of the eye whilst uveo-encephalitis does not. Both give rise to severe generalized uveitis with depigmentary changes in skin and hair. In sympathetic ophthalmia, however, these ectodermal changes occur much less commonly than in the Vogt-Koyanagi-Harada disease. But several cases of sympathetic ophthalmia have been reported with the full clinical picture of the Vogt-Koyanagi<sup>17-19</sup> disease. Occasionally sympathetic ophthalmia may give rise to optic neuritis or inferior retinal detachments as in Harada's disease, but the retina can seldom be seen because of the severe anterior uveitis. It may also cause deafness, fever and signs suggesting meningeal involvement (Duke-Elder).<sup>20</sup> The histological findings in the eye in sympathetic ophthalmia and the Vogt-Koyanagi-Harada diseases are very similar. Harada considered the two conditions to be closely related. Cowper,<sup>7</sup> Swartz<sup>18</sup> and Hager<sup>21</sup> believe them to be identical.

There is, however, one important feature in which the two conditions differ. Typically, sympathetic ophthalmia results from an injury of the eye in which uveal tissue is involved in the wound.

This history is never obtained in Vogt-Koyanagi-Harada disease. However, if both conditions are believed to be due to a virus it is possible that the two conditions may be identical, the only differing feature being the way in which the virus reaches the eyes, i.e. via the blood stream or optic nerves in uveo-encephalitis, and a penetrating wound of the eye in sympathetic ophthalmia. It appears to the authors that sympathetic ophthalmia is but a variant of uveo-encephalitis.

### B. The Allergy Theory

Woods<sup>22</sup> suggested that sympathetic ophthalmia is an allergic reaction to uveal pigment but the evidence is by no means conclusive. In an attempt to determine whether the Vogt-Koyanagi disease has an allergic basis, Rones<sup>23</sup> performed sensitivity tests upon three cases. One test was positive and two were negative. Bruno and McPherson<sup>13</sup> also performed skin tests for allergy to uveal pigment on four patients but their results were negative. Fine and Gilligan<sup>19</sup> obtained a positive reaction to uveal pigment in one case. But the presence of a positive skin test does not necessarily indicate that the disease is caused by allergy to uveal pigment. Since his original suggestion, Woods<sup>24</sup> has pointed out that a similar hypersensitivity reaction to uveal pigment may occur after penetrating ocular injuries.

It may be of some significance that the uveo-meningo-encephalitic syndrome appears to affect the pigmented races such as Negroes and Orientals more frequently than the white-skinned races. Four of our cases were in patients who were of more darkly pigmented racial origin. One was partly Italian, two had Indian blood and one was Chinese.

### TREATMENT

There is no known effective treatment for this condition but there are several reports in the literature which suggest that corticosteroids might be of value. Our second, third and fifth cases were not benefited at all, but the hemiplegia of the fourth patient appeared to show some response when more than double the usual dose was administered. Crawford<sup>25</sup> found cortisone to be of value in one case. Bronstein<sup>11</sup> reported a case in which 20 mg. of prednisone daily produced rapid improvement. A relapse occurred when the prednisone was reduced to 10 mg. daily and there was a rapid response when the dosage was raised to 30 mg. daily. The results in this case and our fourth patient suggest that prolonged and maximal dosage with corticosteroids is required if a satisfactory response is to be obtained. It must not be forgotten, however, that there is a great difference in severity in different cases, the course may fluctuate, and this apparent response may have been due to a natural resolution.

### SUMMARY

The literature of the Vogt-Koyanagi-Harada disease is briefly reviewed.

The essential features of the disease are described. Five cases are recorded.

The etiology and treatment of the condition and its relationship to sympathetic ophthalmia are discussed.

Severe cases may resemble a rapidly expanding intracranial space-occupying lesion. This condition therefore deserves wider recognition to prevent unnecessary exploratory craniotomies.

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### RÉSUMÉ

Le syndrome uvéo-encéphalique que l'on a vu jusqu'à présent surtout dans le domaine des ophtalmologues, se compose d'uvéite, d'achromie de la peau et des cheveux, et de manifestations cérébrales. Les auteurs donnent un rappel historique commençant par Jonathan Hutchinson qui en a fait la description princeps en 1892 bien que son nom ne fasse pas partie de l'appellation éponyme du syndrome. Il est possible que les uvéites bilatérales avec pléocytose du liquide céphalo-rachidien représentent des formes frustes de cette affection. Dans son plein épanouissement l'évolution clinique se répartit en trois phases. La première est la phase méningée caractérisée par des céphalées frontales ou rétro-orbitaires à début brusque et d'une durée de deux à quatre semaines, accompagnées de fièvre. La période ophthalmique suit ou peut aussi se manifester concurremment à la première. On y trouve de la photophobie, du larmoiement, une cécité rapidement progressive et de l'irido-cyclite quelquefois. Le malade

présente des milieux troubles, un œdème rétinien ainsi que des hémorragies et des détachements bilatéraux inférieurs. Une surdité souvent bilatérale mais transitoire avec ou sans bourdonnement peut inquiéter le malade. Le tableau clinique ressemble alors à celui d'une lésion intracrânienne progressive. La convalescence s'amorce à la troisième période pendant laquelle la majorité des lésions disparaissent lentement au cours des mois. Moins de 30% des malades, cependant, recouvrent une vision satisfaisante à cause des complications oculaires (glaucome, cataracte, atrophie optique, contraction du globe oculaire etc.). C'est pendant cette période que l'on voit s'installer la poliose, le vitiligo et l'alopécie. Les faits cliniques de cinq cas sont donnés en guise d'illustration.

Les auteurs s'engagent dans une discussion des deux théories sur l'étiologie de cette affection, à savoir: une infection à virus ou une allergie aux pigments uvéaux. Le gros des preuves semble indiquer une infection virale.

Certaines humeurs injectées au lapin reproduisent la maladie d'assez près; on peut également transmettre d'un animal à l'autre l'affection qui en résulte. On aurait même isolé un virus d'un cas à ses débuts. Il faut se rappeler cependant que les résultats n'ont pas toujours pu être reproduits et sont donc équivoques. Cette théorie d'ailleurs est impuissante à expliquer les manifestations ectodermiques de la troisième période. Le syndrome uvéo-encéphalique a plus d'un trait en commun avec l'ophthalmie sympathique si bien que certains auteurs refusent de voir deux entités nosologiques différentes et prétendent que la seule différence réside dans le mode de pénétration du virus (par blessure dans l'ophthalmie sympathique).

Les bases de la théorie allergique sont très mal établies. La maladie semble s'attaquer plus fréquemment aux individus de races pigmentées qu'aux blancs. Il n'existe aucun traitement spécifique bien que les cortico-stéroïdes aient donné des résultats appréciables.

## THE HAZARDS AND PRINCIPLES OF ANÆSTHESIA FOR TONSILLECTOMY AND ADENOIDECTOMY IN CHILDREN\*

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**TONSILS IN OR OUT?** This is a problem that has troubled the medical profession for many years, and it seems that the question is still unanswered. In England in 1938 a Medical Research Council report regarded the operation as "a prophylactic ritual carried out for no particular reason with no particular result".<sup>7</sup> The truth, of course, is that some benefit does accrue from the removal of some tonsils and adenoids. The possibility that some tonsils and adenoids might just as well be left where they are is purposely stressed not because anaesthetists are often asked to decide this point but, if no great harm is likely to befall a child who retains these items, it is a major catastrophe if some harm does befall him in the process of losing them.

### HISTORY

Hindu surgeons were attacking the tonsils as long ago as 1000 B.C.<sup>1</sup> and Celsus, in A.D. 30, would tear them out with a fingernail.<sup>2</sup> However, the real benefactor of the modern otolaryngologists was a certain Dr. Bosworth, who around 1884 expounded the view that all faecal tonsils were abnormal.<sup>3</sup> Since this time some form of guillotine operation held the field almost until the present day, though Waugh described his technique of blunt dissection in 1909,<sup>4</sup> but taking three minutes to complete, this took at least six times as long as the guillotine operation.

For a long time the operation was performed without anaesthesia and this surprisingly enough was being advocated as recently as 1935.<sup>5</sup> However, though Warren remarked on the use of ether in 1848,<sup>6</sup> general anaesthesia was probably not much in vogue until the 1890s.<sup>2</sup> Two of the favourite techniques were the single-dose method with ethyl chloride or nitrous oxide for the guillotine procedure and ether insufflation of the oropharynx for dissections. Both methods are still widely used.

### PRESENT POSITION

Today the operation still retains much of its popularity, and though the guillotine method is still employed it is gradually giving way to more careful methods of dissection; this paper is therefore concerned mainly with anaesthesia for the latter operation.

In 1954, at a cost to Great Britain of eight and a half million dollars, close upon a quarter of a million children underwent tonsillectomy and/or adenoidectomy,<sup>7</sup> and in Ontario in 1951, 8% of all hospital discharges — medical and surgical — were labelled "hypertrophy of tonsils and adenoids".<sup>8</sup> In the United States the operation is reported as comprising one in four of all surgical operations,<sup>9</sup> and at the Montreal Children's Hospital it comprises around 28% of all operations on children.<sup>10</sup>

With this long history and high incidence, it is surprising that Collins and Granatelli were able to write in 1956, "The most neglected of anaesthetic procedures is that for tonsillectomy",<sup>11</sup> and in spite of the number of articles which have recently appeared on this subject, their remarks still contain more than a grain of truth.

### HAZARDS

In 1955 in Canada, 27 children under 15 years of age died, and tonsillectomy and adenoidectomy appeared on the death certificate.<sup>12</sup> In a review from a town in the United States of 20,000

\*A paper prepared for the McGill University Diploma Course in Anæsthesia, and read before a meeting of Anæsthetists of Montreal on March 3, 1958.

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operations performed over 30 years, there was an incidence of one death per 2200 cases.<sup>13</sup>

The causes of mortality and morbidity are not well documented, but some facts are available. Of a series of 750 deaths associated with anaesthesia investigated by a committee in England, ten were also associated with tonsillectomy and/or adenoidectomy.<sup>14</sup> Five of these were associated with anaesthesia for postoperative haemorrhage. Of the other five, four probably died as a result of blood in the bronchial tree. By merely talking to 26 anaesthetists (half of whom are still in training) here in Montreal, it has been possible to obtain information on 12 deaths associated with this operation, though these were not by any means all firsthand experiences. Of these, five died from postoperative haemorrhage, and five appeared to have died from cardiac arrest, with or without anoxia and/or anaesthetic overdosage. The eleventh inhaled a clot and asphyxiated and the twelfth was accidentally insufflated with liquid ether. In collecting these few cases, it was impossible not to note the number of "near misses" that occurred.

Of postoperative complications, Waldapfel<sup>15</sup> states that haemorrhage is the commonest and that lung complications follow this in frequency. Formerly, pulmonary abscess was frequently reported as a sequel to the operation, but it is almost unheard of now. However, Waldapfel states that small areas of atelectasis have been demonstrated postoperatively and are probably more common than we think and may account for a number of cases of postoperative fever. Finally psychological trauma, manifest by night terrors, bed-wetting and the like, has been quoted as a sequel to a stormy visit to hospital for the operation in question.<sup>16</sup>

#### MANAGEMENT OF THE ANÆSTHETIC

*Preparation of the patient* for operation starts even before he is admitted to hospital, and can be considered as psychological and pharmacological.

The psychological aspect engulfs all the problems associated with the admission of children to hospital, for often this particular admission may be their first encounter with hospitals and is also often the first separation of the child from its parents. Much has been written of the ways to reduce psychological trauma, but it would seem that there is little better than commonsense handling at this stage. Though no-one would desire the child to be thoroughly terrified, it is also of importance that children learn to cope with some of the less pleasant experiences in life, and it should not be forgotten that even young children are often able to understand a simple explanation of what is in store for them. It is probably equally important that the parents should receive a similar explanation, in order to dispel their anxiety, which is often very contagious to their children.

That these children should be admitted to hospital is less debated than formerly, but in some hospitals children for this procedure are still ambulatory, arriving a half to one hour before operation. This allows time neither for any physical assessment nor for the child to get used to his new environment. One is not certain that milk or the like has not been recently administered by a compassionate mother. There is no time for a pre-operative visit by the anaesthetist, so that after being torn screaming from its mother's arms and dumped on the operating-room table, the child's first encounter with this individual is when he descends upon him in cap, mask and gown, brandishing an ethyl chloride spray in one hand and a Schimmelbusch mask in the other.

The aims of pharmacological preparation are little different for this operation than for any other procedure, whether it be in adult or child, viz. to lessen secretions and to allay fear and apprehension, thus augmenting the effect of psychological preparation.

The first aim is relatively easy to satisfy by the administration of atropine or hyoscine according to taste, though in addition to the advantage of its central depressant effect, the latter drug has recently been shown to be a better drying agent.<sup>17</sup> The second aim is not so easy to satisfy, for adequate preoperative sedation often leads to depression during induction and maintenance and in the postoperative phases. Many agents have had their vogue, but usually the choice lies between no premedication other than atropine and the use of a barbiturate or an opiate. The first alternative seems inhumane, for even with the best of good intentions to put on a brave face, some children do break down at the last minute. With adequate dosage of a barbiturate such as pentobarbitone, the child can be sent to sleep in his ward, but this effect tends to be unpredictable, the drug has an unpleasant taste and anyway such dosage tends to make some children unduly depressed, both during induction and maintenance, and in the postoperative phase may cause either depression or undue restlessness. Rectal thiopentone<sup>18</sup> is undoubtedly better in all respects, but children who have received this require very careful pre-operative supervision. The objection that it is a gross assault upon the child would seem to be invalid, and there is one head nurse who obtained excellent results by merely pointing out that the medicine did not taste nasty given that way. Opiates are tolerated well by children in appropriate dosage, but there are some who consider Anderson's scale of doses<sup>19</sup> to cause too much post-operative depression for use in tonsillectomy cases. For those who hold this view, Leigh and Belton's scale of doses<sup>20</sup> may be used one hour pre-operatively. A small dose of pentobarbitone half an hour before this injection enhances preoperative sedation, and the inclusion of an analgesic appears to pay dividends in the postoperative phase. The

dose of pentobarbitone required is 16 mg. for children from one to three years, 30 mg. from four to seven years, and 60 mg. from eight to twelve years.<sup>21</sup>

Timing of the premedication is as important in this operation as it is in any other, and to be admitted into the anaesthetic room accompanied by a nurse he knows is added security for the child. The operation, if possible, is best scheduled for the morning, for a child may put up with missing his breakfast, but to be deprived of his lunch as well is often too much, especially if other children in the ward are enjoying theirs. Likewise, it is bad for morale for children awaiting operation to witness the recovery of those who have already been through the process.

### *Induction*

Ideally this is a quiet and peaceful procedure and is achieved by a skilful intravenous injection<sup>24, 25</sup> or a delicate wafting of nitrous oxide or cyclopropane before the child's nostrils. Both procedures are more successful if accompanied by a constant hypnotic discourse from the anaesthetist, absolute silence being observed by any onlookers, for an untimely word from these quarters will divert the child's attention and may cause several minutes' additional hard work. The only special problem to be borne in mind at this stage is the possibility of upper respiratory obstruction occurring, due to the enlarged tonsils and adenoids. It may also be mentioned that ethyl chloride does not appear to be the innocuous agent so many people believe it to be.<sup>22</sup>

### *Maintenance*

It is at this phase that the most controversial matter is reached. It is not intended to discuss the relative merits of various agents, for this is really a very minor matter. Almost any agent can be employed and the choice is really the choice of the administrator, his aim being to avoid over-dosage and anoxia and to have his patient virtually awake with all the vital laryngeal and pharyngeal reflexes active at the end of the operation. In addition, perfect control of the airway must be achieved and it is over this point that controversy rages.

The established method has been to position the child's nasopharynx lower than the larynx and by some device or other to hold the tongue forward. Ether and oxygen or air are then insufflated into the airway. The modern trend, advocated for many years in some quarters<sup>23</sup> but stressed in recent articles, is to pass an endotracheal tube.<sup>24, 25</sup>

To assess the merits of the two methods it would be as well to review the anaesthetic requirements of the stage. They are:

1. To maintain a clear airway—rule number one for all anaesthetics.<sup>26</sup> This is necessary to allow free access of oxygen and anaesthetic vapours to the alveoli and to allow egress of carbon dioxide.

Also it is necessary to have a clear route for the administration of oxygen in emergency.

2. To prevent access of blood and debris to the larynx, trachea and bronchi, in order to prevent asphyxia and postoperative lung complications.

3. To have sufficient control over the depth of anaesthesia, in order to avoid overdosage with the agent, to keep anaesthesia tranquil and to have the child virtually awake at the end of the operation.

It will be remembered that the particular hazards of this operation are: (a) haemorrhage during and after the operation, of sufficient amount to cause death on occasion; and (b) inhalation of blood or debris, again on occasion sufficient in amount to cause death. Finally, Stephen<sup>27</sup> states that the greatest single cause of death in paediatric anaesthesia is anoxic anoxia, and he points out how even a small obstruction is relatively severe in the small airway of the child.

How then does the insufflation method meet these requirements? It would not appear to meet any of them.

1. It does not maintain a clear airway, for the surgeon is working right in the centre of this, normally the anaesthetist's most jealously guarded territory. Laryngeal stridor often occurs or even gross coughing when the patient is light, and respirations are often shallow and feeble when the patient is deep. A minor obstruction due to a tiring assistant's allowing the neck to flex or the tongue to fall back, inevitably results in some degree of anoxia. Signs of this anoxia may not be very easy to detect if, as is often done, the surgeon insists on working in the dark. Finally, strain what oxygen is reaching the patient through a bloody gauze swab in the oropharynx, and it becomes but a very short step to cardiac arrest.

Collins and Granatelli<sup>11</sup> showed with some oximetric studies that, near the termination of three insufflation anaesthetics, oxygen saturation of the arterial blood was around 75-80%.

Lowenthal<sup>28</sup> has shown that pharyngeal secretions enter the larynx during deep anaesthesia, and several other workers have demonstrated a high incidence of bloody secretions in the trachea and bronchi after tonsillectomy and adenoidectomy.<sup>29-33</sup> Small amounts of blood are probably harmless, but if small amounts can enter so can large amounts in the event of haemorrhage getting out of control, and so also can infected debris.

3. By this method it is necessary to anaesthetize the patient fairly deeply in order that coughing may be eliminated. If this is not achieved, it is very difficult to deepen the anaesthetic during the course of the operation. It is also easy to produce apnoea by having the patient too deeply anaesthetized, especially at the beginning of the operation.

How, on the other hand, does endotracheal anaesthesia meet these requirements?

1. As far as is humanly possible under the circumstances, it maintains a clear airway and allows artificial ventilation to be performed at will.

2. By the choice of a snugly fitting tube it is possible to prevent access of blood in any quantity or debris into the trachea; should blood find its way in, it can be readily aspirated.

3. It has been shown that with endotracheal anaesthesia, anaesthesia can be maintained with lower blood concentrations of ether.<sup>34</sup> Over-dosage is therefore less liable to occur, and if it does there is a reservoir bag to indicate this in a dark operating room. Should coughing occur, there is a patent airway available to deepen anaesthesia. Other advantages are that with the use of a short-acting relaxant induction time is greatly shortened from the minimum of seven minutes required for the insufflation method, and also a modern technique of so-called "balanced anaesthesia" may be employed, if desired.

The objections to endotracheal anaesthesia are many. Some surgeons say that the tube gets in their way, but many other surgeons manage quite well by moving the tube from one side of the mouth to the other. An improvement on this method would seem to be the use of the modified Boyle-Davis gag described by Doughty.<sup>24</sup> This hides the endotracheal tube in the midline under the tongue spatula and also prevents any trauma or stimulation of the larynx, which may occur from movement of the tube during operation. Nasal intubation also has the advantage of not stimulating the larynx, but there is a real danger of damaging the adenoids, causing profuse bleeding when it is passed, and it is not possible to use as large a tube as by mouth. It is also claimed that trauma may occur to the larynx after intubation, but at least three separate series<sup>25, 35, 36</sup> amounting to over 12,000 cases have been reported with no permanent laryngeal sequelæ. If Smith's<sup>35</sup> recommendations for avoiding mechanical trauma, chemical trauma, and bacterial contamination are followed, it seems likely that others could produce similar results. Stridor is not an uncommon complication, but in one series<sup>11</sup> it was nearly three times as frequent after the use of an insufflation technique. A further objection is that an endotracheal tube increases the airway resistance, and in fact the resistance is inversely proportional to the fifth power of its diameter.<sup>37</sup> At a flow rate of one litre per minute a No. 9 Magill tube increases the normal resistance of the upper respiratory tract seven times.<sup>38</sup> However, in practice no great harm seems to arise; should the anaesthetist feel strongly about the matter, he can always saddle himself with the extra burden by assisting respiration.

As mentioned earlier, it is not intended to discuss specific agents used for maintenance, but some mention must be made of the use of relaxants. These do not seem to be contraindicated, provided: (a) an endotracheal tube is used; (b)

the duration of action of the relaxant chosen suits the duration of the operation, so that full muscle power has returned at the end of the procedure; and (c) adequate ventilation is ensured. The latter requirement almost certainly entails assisting respiration, and it could be argued that raising the venous pressure by this means might cause increased oozing of the operation site.

Finally, it is often argued that the insufflation technique has stood the test of time, but one wonders whether this is true. Anaesthetic deaths are still too numerous for this elective operation, and it is difficult to escape the conclusion that insufflation methods no longer satisfy the high standards demanded of modern anaesthesia.

#### *The Postoperative Phase*

At the end of the operation it is desirable for the patient to have complete control of his airway, and it should therefore be the aim to have the child virtually awake at the end of the procedure. In this way, vital laryngeal and pharyngeal reflexes are present to protect against the hazards of this phase of the operation, namely aspiration of blood or obstruction of the airway by the tongue. This is undoubtedly the greatest safeguard we can offer the patient, but failing this he should be allowed to recover in the semi-prone position, without a pillow under the head. In this way blood drains out of the mouth instead of into the larynx, and the tongue falls away from the posterior pharyngeal wall.

Sedation in this stage is also a vexed question, but with light premedication and anaesthesia, may be necessary. If the child is well awake, it would seem that small doses of meperidine (Demerol) are innocuous and being analgesics are more effective than the traditional use of hypnotic. A careful pulse record must be kept during this stage in order that signs of postoperative haemorrhage may be detected, for children often swallow the blood and a rising pulse is the first sign that all is not well.

Finally a short description of the operation is of note. It is that of a surgeon named Sharn, who, trying to popularize the operation in 1750, said, "It is neither dreadful in the doing, nor melancholy in the event."<sup>39</sup> We might do worse than appropriate these words and apply them to our anaesthetic method.

#### **SUMMARY**

The possibility that the operation of tonsillectomy and/or adenoidectomy in children may sometimes be unnecessary is stressed, in order that anaesthetists should appreciate the catastrophic nature of any death occurring as a result of the procedure.

A short résumé of the history of the operation is presented.

An attempt is made to give some idea of the frequency of the operation and of the incidence of death resulting from it. The main causes of morbidity and mortality are presented.

The management of the anaesthetic is discussed. The problems associated with premedication are considered and a critical evaluation of the cases for and against endotracheal intubation in this operation is presented, with the conclusion that insufflation methods no longer satisfy the high standards required of modern anaesthesia.

Brief mention is made of some of the postoperative problems.

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#### RÉSUMÉ

L'auteur insiste sur l'importance d'une indication chirurgicale réelle pour l'ablation des amygdales et des adénoides, étant donné la nature désastreuse de toute catastrophe encourue durant ou après l'opération.

Un bref historique de l'opération est inclus dans l'article, l'origine de l'intervention remontant à l'an 1,000 avant J. C. L'intervention est encore de nos jours très pratiquée, mais au Canada en 1955, vingt-sept morts chez les moins de quinze ans lui sont attribuables. Les principales causes de mort sont l'hémorragie, l'inhalation de sang et l'arrêt cardiaque en cours d'anesthésie. Cette dernière complication peut être la résultante d'une surdose d'agent anesthésique, de l'anoxie ou d'une action simultanée de ces deux facteurs. Des complications pulmonaires mineures sont possibles pendant la période post-opératoire.

La préparation préopératoire de l'enfant devrait être à la fois psychologique et pharmacologique. Sous ce dernier rapport il est considéré inhumain de ne pas user d'un sédatif dans la prémédication. Il est cependant important d'éviter une dépression trop grande de l'enfant.

Les problèmes relatifs au maintien de l'anesthésie, le pour et le contre de l'intubation sont discutés à fond, avec la conclusion que l'ancienne méthode d'anesthésie par insufflation n'atteint plus le haut standard requis par l'anesthésie moderne. Sans intubation endotrachéale, l'anesthésiologue n'a un contrôle adéquat, ni de la perméabilité des voies respiratoires, ni de l'agent anesthésique. Un degré plus profond d'anesthésie est requis chez les patients non intubés, l'anoxie s'installe plus aisément et les débris ont plus facilement accès au larynx.

Plus de 1,200 cas sont rapportés, chez lesquels l'intubation a été employée sans aucun trouble permanent.

En terminant l'auteur insiste sur l'importance d'obtenir d'actifs réflexes laryngien et pharyngien à la fin de l'opération.

F.R.H.W.

## THE ASSESSMENT OF THE CERVIX AT SURGICAL INDUCTION\*

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SINCE 1952, when Gibson<sup>1</sup> reported upon a series of surgical inductions from Belfast, several publications have appeared in the British literature which reflect a renewed interest in the subject. It is generally accepted that the success of an induction is dependent upon the ripeness of the cervix, but two of the recent writers (Evans,<sup>2</sup> Parker<sup>3</sup>) raise doubts about the value of the traditional view. On the other hand, Cocks<sup>4</sup> reported a series of 133

cases in which the initial condition of the cervix was carefully studied, and he concluded that by doing so "the clinician can learn much that will help him in the subsequent care of his cases".

The present investigation was planned in order to determine whether or not the condition of the cervix at surgical induction really influenced subsequent events; to do so, the method of classifying the cervix recommended by Cocks was employed. Six types of cervix are described, and these are explained by the accompanying diagrams and legends. Furthermore, it was considered that many other factors could influence the course of labour after induction, notably age, parity, gestation period, station of the presenting part, type of induction, character and amount of liquor, and the primary condition necessitating induction. Such additional data were collected to assist the final analysis.

\*This investigation was carried out in the University Unit of Obstetrics, City General Hospital, Sheffield, England.  
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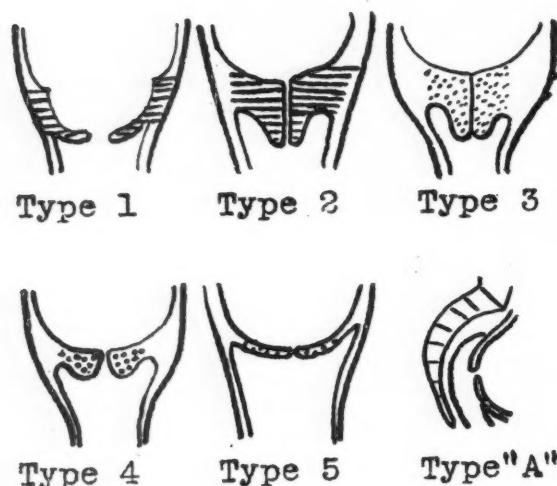


Fig. 1.—Types of cervix uteri (after Cocks).

Type 1.—Soft, effacing, canal admits one finger.

Type 2.—Soft, long and closed. Whole canal admits one finger.

Type 3.—Firm, long and closed. External os will not admit one finger.

Type 4.—Firm and short. External os admits one finger. Internal os rigid.

Type 5.—Cervical anomaly. Pin-hole os.

Type "A".—Sacral os. Anterior sacculation occurring in any of the previous types.

#### MATERIAL

In this study, 274 cases of indicated inductions were observed. The cervix was classified at the time of surgical induction, which was performed by hindwater or forewater puncture. Hindwater puncture was generally favoured, but no particular policy was followed, so that there were 194 hindwater punctures and 80 forewater punctures, the latter being performed by accident in some cases, or because of failure to perform hindwater tap, or simply for a change.

#### RESULTS

The distribution of the types of cervix is shown in Table I, which shows that the Type 2 cervix was the most common, and that 75.9% of cases were "ripe" (Types 1 and 2), and 24.1% were "unripe" (Types 3, 4, 5, and A). The distribution as reported by Cocks is also tabulated for the purpose of comments to be made later.

The relationship of the type of cervix to the induction-delivery interval (I.D.I.) was examined (Table II), and it was found that whereas only 14.4% of the "ripe" cases were still undelivered after 72 hours, 39.4% of the "unripe" cases were not delivered, and this difference is statistically significant ( $\chi^2 = 18.5$ ;  $p = \text{less than } 0.001$ ). Thus, provided no sources of bias can be demonstrated which could invalidate the comparison, it seems that the condition of the cervix at the time of induction is of some prognostic value.

It is also seen (Table II) that the Type 1 cervix appears to be the most favourable, followed

TABLE I.—DISTRIBUTION OF CASES ACCORDING TO TYPE OF CERVIX.

Type	Present investigation Cases	Percentage	Cocks' series Cases	Percentage
1	70	25.5	66	49.6
2	138	50.4	23	17.3
3	19	6.9	4	3.0
4	37	13.5	5	3.7
5	2	0.7	1	0.8
A	8	3.0	34	25.6
Totals.....	274	100.0	133	100.0

TABLE II.—INDUCTION-DELIVERY INTERVAL IN RELATION TO TYPE OF CERVIX

Type	<24 hours		24-48 hours		48-72 hours		>72 hours	
	No.	%	No.	%	No.	%	No.	%
1	51	72.8	9	12.9	7	10.0	3	4.3
2	78	56.5	22	16.0	11	8.0	27	19.5
3	3	15.7	3	15.7	4	21.1	9	47.5
4	10	27.0	10	27.0	5	13.5	12	32.5
5	—	—	—	—	1	50.0	1	50.0
A	1	12.5	—	—	3	37.5	4	50.0
Totals	143	52.2	44	16.1	31	11.3	56	20.4

by the Type 2 cervix (97.7% and 80.5% respectively being delivered within 72 hours); cervix Type 4 appears to occupy an intermediate position (67.5% delivered within 72 hours); whilst Types 3, 5, and A appear to be the least favourable (collectively, only 46.9% delivered in less than 72 hours).

The data were next examined to determine to what extent abnormal uterine action was responsible for the prolongation of the induction-delivery interval. It was found that there was mainly a close correlation between the induction-labour interval (I.L.I.) and the induction-delivery interval (I.D.I.) (Table III).

TABLE III.—RELATION OF INDUCTION-LABOUR INTERVAL TO INDUCTION-DELIVERY INTERVAL

Type	Less than 24 hours	24-48 hours	48-72 hours	More than 72 hours	Totals
1 I.L.I.	59	9	3	2	70
	51	9	7	3	
2 I.L.I.	94	14	6	24	138
	78	22	11	27	
3 I.L.I.	6	3	2	8	19
	3	3	4	9	
4 I.L.I.	13	9	4	11	37
	10	10	5	12	
5 I.L.I.	1	1	0	0	2
	0	0	1	1	
A I.L.I.	4	0	1	3	8
	1	0	3	4	

Therefore it seems that once uterine contractions commence after surgical induction, labour usually progresses normally regardless of the duration of the induction-labour interval. There were, in fact, only 12 cases of abnormal uterine action in the present series, but it was most striking to note that 10 of these cases were classified as "unripe" at the time of induction. The difference between the incidence of prolonged labour in the "unripe" group (15.2%)

and the "ripe" group (0.9%) is statistically significant (Chi square = 23.9,  $p$  = less than 0.001).

There was further evidence to show that, provided good contractions became established soon after induction, the patient with the unripe cervix might be expected to deliver herself. This was reflected by the incidence of operative deliveries. The incidence of indicated forceps delivery was 7.2% in the cases with ripe cervix and 12.1% in those with an unripe one, a difference not statistically significant. The incidence of Cæsarean section was 1.5% in both groups, but whereas no cases with a ripe cervix underwent section for inertia, this was the most common indication in the unripe cases.

#### AGE

There was some evidence to suggest that youth favourably influenced the outcome of surgical induction. Thus, only 10% of the patients aged 20 or under remained undelivered after 72 hours, the comparable figures for the 21-25, 26-30, 31-35 and 36-40 age groups being 19.5%, 18.6%, 27.9% and 41.6%. These results are not statistically significant, and although there does seem to be a trend towards a longer induction-delivery interval with increasing age, the influence of age does not appear to be as striking as the initial condition of the cervix. This was further illustrated when the cases with unripe cervix were re-examined to see whether those patients who responded well were in the younger age groups, but this was not the case and age appeared to be of no particular significance in this group.

#### PARITY

After 72 hours, 22.5% of the primigravidæ and 18.6% of the multigravidæ were still not delivered, a difference which is not significant. Looked at another way, there was no evidence to suggest that the primigravidæ responded any less readily to induction than the multigravidæ (48.6% and 56.8% respectively being in labour within 24 hours, the difference is not significant). Thus, parity does not seem to be an important factor influencing the induction-delivery interval.

#### GESTATION PERIOD

It is frequently assumed that the nearer to term the membranes are ruptured, the greater the likelihood of a prompt response. The evidence of the present survey does not lend strong support to this view, for although at 34 weeks (and less) 31.2% were still undelivered after 72 hours, the results at 35-38 weeks, 39-41 weeks and 42 weeks or more were 28.6%, 22.4%, and 10.7%. The type of cervix was seen to be a more reliable guide; for instance, a ripe cervix at 34 weeks was a good omen as regards response, whilst an unripe cervix at 42 weeks was a bad sign.

#### VOLUME AND CHARACTER OF THE LIQUOR

The percentage of cases undelivered after 72 hours after 10 fluid ounces or less, 11-20 fluid ounces, 21-30 fluid ounces or 31 fluid ounces or more of liquor amnii had been removed was 14.8%, 23.4%, 22.9% and 30% respectively. These differences are not significant, but it may be that, if less than 10 fluid ounces is removed (or less than 10 fluid ounces is available), the response to induction is more prompt than otherwise.

Manly<sup>5</sup> suggested that the finding of vernix-laden liquor might be a favourable sign, but there was no definite evidence to confirm this. Where the liquor was clear, 22.7% of cases delivered after 72 hours, compared with 14.5% of those with much vernix (the difference is not significant).

#### STATION OF THE PRESENTING PART

It was thought that the relation of the presenting part to the pelvic brim might be of some prognostic value, since the formation of the lower uterine segment probably influences the normal engagement of the fetal head.<sup>6</sup> It was found that where the presenting part was fixed, 18% of cases took longer than 72 hours to deliver whilst 26.6% of those with a free presenting part were undelivered at this time. This difference is not significant.

#### RESULTS OF INDUCTION IN SPECIFIC CONDITIONS

Table IV shows some of the features of induction for pre-eclampsia, postmaturity, and accidental haemorrhage. At first appraisal it seemed that postmaturity or accidental haemorrhage predisposed to a good response. However, it should be pointed out that in the case of postmaturity, a degree of selection of cases was exercised so that only 13 of the 76 cases had an unripe cervix. In the case of accidental haemorrhage, several of the 19 cases may have been in early labour; certainly only 2 had an unripe cervix.

TABLE IV.—INDUCTION IN SPECIFIC CONDITIONS

	Cases not delivered within 72 hours	Total	Percentage
All cases in present series	56	274	20.4
Severe pre-eclampsia . . . . .	1	5	20.0
Moderate pre-eclampsia . . . . .	8	27	29.7
Mild pre-eclampsia . . . . .	23	90	25.5
Postmaturity . . . . .	8	76	10.5
Accidental haemorrhage . . . . .	2	19	10.5

#### HINDWATERS OR FOREWATERS?

The case records were examined in an effort to determine whether a better response was obtained by rupturing the hindwaters or the forewaters. It was found that 23.7% of cases in which the hindwaters were punctured were undelivered after 72 hours, compared with 12.5% of those with forewater rupture; this difference is significant (Chi square = 4.17, " $p$ " less than 0.05). It would

TABLE V.—HINDWATER PUNCTURE AND FOREWATER RUPTURE  
(Cases delivered more than 72 hours after induction).

	Types 1 and 2 cervix			Types 3, 4, 5 and A cervix			All cases		
	No.	Total	%	No.	Total	%	No.	Total	%
Hindwaters	25	139	17.9	21	55	38.2	46	194	23.7
Forewaters	5	69	7.2	5	11	45.4	10	80	12.5

be wrong to conclude that this means necessarily that forewater rupture was the most efficient procedure, for if the distribution of ripe and unripe types of cervix was different in the two groups, this source of bias would invalidate the comparison. This difficulty can be overcome simply by making the comparison again but with the ripe-cervix cases (Types 1 and 2) separated from the unripe-cervix cases (Types 3, 4, 5, and A). In the ripe cases, 17.9% of the cases of hindwater puncture and 7.2% of the cases with forewater rupture were delivered after 72 hours; this difference is significant (Chi square = 4.38, "p" less than 0.05). In the unripe-cervix cases, the ratio was 38.2% of hindwater punctures and 45.4% of forewater ruptures. At first sight, it seems as if the efficiency of the methods is reversed in the cases with an unripe cervix, but the difference in the latter group is not significant. But the interesting fact emerges that if the cervix is ripe, the response to induction is more satisfactory with forewater rupture whereas, if the cervix is unripe, it seems that such an advantage is not maintained (Table V).

#### DISCUSSION

On the whole, the Cocks classification of the types of cervix was found to be adequate. There were few cases in which there was any real difficulty in assigning any particular cervix to one of the six possible types, but there were examples such as the cases of genuine difficulty in deciding whether a cervix was Type 2 or Type 4. In such circumstances, the less favourable type was chosen. Nevertheless, the distribution of the cases in the present series differed in some respects from that reported by Cocks (Table I), the most important differences being the almost complete reversal between the Type 1 and Type 2 cases, the slightly greater incidence of Type 4 cases, and the greatly reduced incidence of the cases of "sacral" cervix (Type A).

In the case of Types 1 and 2, the difference was most likely due to the prior use of digital stripping of the membranes and stretching of the cervix, for no fewer than 191 of the 274 cases in the series (69.7%) had failed to respond to this method of induction, whilst many cases went into labour after such treatment and do not therefore appear in the series. Unfortunately, a complete record of these cases was not kept, but it is probably safe to assume that they comprised mainly cases with the most favourable type of cervix (Type 1).

Regarding the Type 4 cases, it may be that the policy of allotting to this group doubtful cases

of Type 2 cervix created the apparent greater incidence, and this would explain why some of these cases responded more favourably than was expected. On the other hand, there is no obvious explanation for the markedly lower incidence of sacral cervix in this series, but it is possible that the interpretation of this condition was less liberal, which may provide a clue to the unexpectedly poor performance of a few of the "ripe" cases.

Despite these limitations, the system of typing the cervix does seem to have definite prognostic value, and from the evidence of this series it can be said (in round figures) that 95% of Type 1 cases, 80% of Type 2 cases, 65% of Type 4 cases, and 50% of Type 3, 5, and A cases will be delivered within 72 hours of induction by liquor loss. Also, the chances of abnormal uterine action developing in cases of ripe cervix is exceedingly low (0.9%) compared with the cases of unripe cervix (15.2%). Moreover, these statements of prognosis could only be produced from a study of the initial condition of the cervix, since there was but scanty evidence that age, parity, gestation period, the volume and character of the liquor removed, the station of the presenting part, or the primary indication for induction had anything like such an influence on the outcome.

The question arises "To what extent should the nature of the initial condition of the cervix influence the decision to induce labour?" Now a necessary induction will always be necessary and an unnecessary induction will always be unnecessary, but it would be unwise therefore to conclude that the condition of the cervix should not influence the decision at all, because there are very many cases in which the decision must be in the balance. In such cases, the evidence is strong enough to encourage one to go ahead with Type 1 and 2 cases, but to procrastinate with the rest. If the indication for induction is very urgent, however, even if the cervix is unfavourable, one should not be put off, because it has been shown that even 65% of Type 4 case and 50% of Types 3, 5, and A cases will be safely delivered inside 72 hours, so that the procedure is well worth while.

The knowledge that some 15% of cases with an unripe cervix will develop incoordinate uterine action is perhaps a less helpful piece of information, since this is usually apparent within 24 hours of induction regardless of the initial condition of the cervix. Nonetheless, one can imagine circumstances where this observation could influence a decision.

The initial state of the cervix may also indicate the type of induction to be employed. Once the decision to rupture the membranes has been made, it seems clear that if the cervix is Type 1 or 2, forewater rupture may be expected to produce a quicker response. This has to be balanced against the alleged advantages of hindwater puncture, namely, less infection, less risk of cord prolapse, and better labour because of the intact forebag. Regarding infection, there was no evidence in the present series that hindwater puncture conferred any benefit. On the contrary, the infection rates were 7.2% and 3.8% in favour of forewater rupture—this despite the fact that the 1.5% incidence of prophylactic chemotherapy was confined, curiously enough, to cases of hindwater tap. There were no cases of cord prolapse in the present series, and I believe that the safety of hindwater puncture in this respect has been overrated. The incidence of abnormal uterine action was not significantly different in cases of high puncture (4.1%) and of low rupture (5%). On the other hand, the present investigation contained one case of fetal death due to placental damage with a Drew Smythe catheter; similar cases have been described elsewhere.<sup>7</sup> Moreover, this instrument yielded a "bloody tap" in 10.5% of cases which seemed later to be associated with an abnormally high incidence of postpartum haemorrhage.<sup>8</sup> Hindwater puncture has never been popular in North America, and the foregoing evidence would appear to endorse this. The main virtue of the Drew Smythe catheter, as I see it, is that it is a handy instrument for rupturing the forewaters. It is probable that had forewater rupture been favoured in the present series, the results in the ripe cases would have been better, particularly in Type 2 cases. As it was, 19.5% were delivered after 72 hours, but of the 94 cases treated by hindwater puncture in this group, 21 (22.3%) took longer than 72 hours to deliver, compared with 6 out of 44 (13.6%) treated by forewater rupture.

The position with regard to the cases of the unripe cervix is by no means so clear-cut. From the evidence available, it seems likely that no great improvement can be expected from the use of forewater rupture. It is probable that better results in these cases may be obtained by means of Pitocin. Intravenous infusions of Pitocin (or Syntocinon) were used on only 18 occasions in the present series, six times in an attempt to ripen the cervix before rupture of the membranes, ten times for failure to start labour after 48 hours, and twice for inertia. Although this infrequent use of the Pitocin drip increased the value of the survey in relation to the natural history after membrane rupture, it provided little opportunity to judge the effectiveness of Pitocin in influencing the clinical course. A Pitocin drip may be used in several ways in relation to surgical induction of labour: it can precede membrane rupture in an attempt to ripen the cervix; it can be set up as a routine at the time of surgical

induction; or it can be used after membrane rupture in those cases where labour has not started after a reasonable interval. The most rational approach would appear to be that recommended by Nixon and Smyth,<sup>9</sup> in cases with a ripe cervix, surgical induction is performed, and a Pitocin drip is reserved for: (a) those cases which are insensitive to an intravenous test dose of 0.03 units of Pitocin, and (b) those cases not in labour after 24 hours. In cases with an unripe cervix, the drip is used to ripen the cervix before rupture of the membranes.

#### SUMMARY

The condition of the cervix was assessed before 274 surgical inductions. The classification of Cocks into Types 1 and 2 (ripe) and Types 3, 4, 5, and A (unripe) of cervix was used.

The subsequent performance of the cases was studied in relation to the patient's age and parity, to the gestation period, the character and volume of liquor removed, the station of the presenting part, the type of induction and the primary indication for the induction.

It was found that only the initial condition of the cervix and the type of induction had any great influence on the outcome.

The induction-delivery interval was mainly closely related to the induction-labour interval.

Of the cases with a Type 1 cervix, 97.7% were delivered within 72 hours compared with 80.5% of Type 2, 67.5% of Type 4, and 51.7% of Types 3, 5, and A. The performance of the cases with a ripe cervix was significantly better than those with an unripe cervix.

The incidence of abnormal uterine action was significantly greater in the cases with an unripe cervix (15.2%) than in cases with a ripe cervix (0.9%). There was no evidence that cases with an unripe cervix were more likely to require operative delivery provided uterine action was normal.

The efficiency of forewater rupture over hindwater puncture was demonstrated in the cases with a ripe cervix, but was not demonstrated in the cases with an unripe cervix. Other reasons were advanced in favour of forewater rupture.

It is suggested that the procedure of carefully assessing the cervix may influence the decision regarding induction, can be of general assistance in formulating a prognosis, and may help in the evaluation of individual cases.

I wish to record my thanks to Professor C. Scott Russell for allowing me to conduct this study in his department, and for his encouragement and advice at all times.

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**LONG-TERM USE OF PREDNISONE  
(Meticorten) IN GENERALIZED  
CASES OF LUPUS ERYTHEMA-  
TOSUS, SCLERODERMA AND  
NEURODERMATITIS DISSEMINATA**

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THE STEROIDS, along with modern antibiotics, have contributed greatly to furthering our knowledge of the pathogenesis and therapeutics of many diverse disabling diseases. The year 1950 marked an important milestone in modern dermatology as a result of the apparent favourable response of infantile eczema to ACTH.<sup>1</sup> Subsequently dermatologists have become cautious and even timid in the use of corticosteroids orally and parenterally because of the great mass of literature which has accumulated indicating its potential dangers. Great strides nevertheless have been made in reducing the morbidity of many dermatoses by the topical application of these hormones. But there still remained a problem of management of such serious and formerly rapidly fatal diseases as acute lupus erythematosus disseminatus (systemic) and pemphigus. It is here that the systemic use of corticosteroids has made such a major contribution in reducing the morbidity and favourably influencing the mortality rate.

Other major problems common to dermatologists, internists and general practitioners have been the management of the totally disabling generalized neurodermatitis disseminata and generalized scleroderma. The threat of unfavourable complications from the large maintenance dose of ACTH, cortisone and hydrocortisone required has been a deterrent to their long-term use in relatively benign recurring conditions. Our interest was rekindled following the work of Bumim *et al.*<sup>2</sup> on the use of prednisone (Meticorten) and prednisolone (Meticortelone) in rheumatoid arthritis. Their work indicated that the synthetic analogues of cortisone and hydrocortisone were two to four times more effective as antirheumatic and antiphlogistic agents. However, there was no corresponding increase in toxicity and their cases could be carried in comfort on doses ranging from 5 to 25 mg. daily. On this dosage no electrolyte disturbances were noted. Subsequently it was pointed out<sup>3</sup> that major undesirable side effects, e.g. peptic ulcers and severe psychoses, can result from prednisone and prednisolone therapy.

Since March 1955, we have had the opportunity for a close clinical and laboratory study of prednisone (Meticorten) in three disabling dermatomedical conditions and feel that the favourable response on the dosage used merits the present report.

The purpose of this study was to determine:

1. The feasibility and efficacy of long-term therapy with prednisone (Meticorten) in the following chronic diseases: lupus erythematosus disseminatus (systemic), generalized scleroderma (systemic) and generalized neurodermatitis disseminata (atopic eczema).

2. The risks involved in such long-term therapy.

**CASE REPORTS**

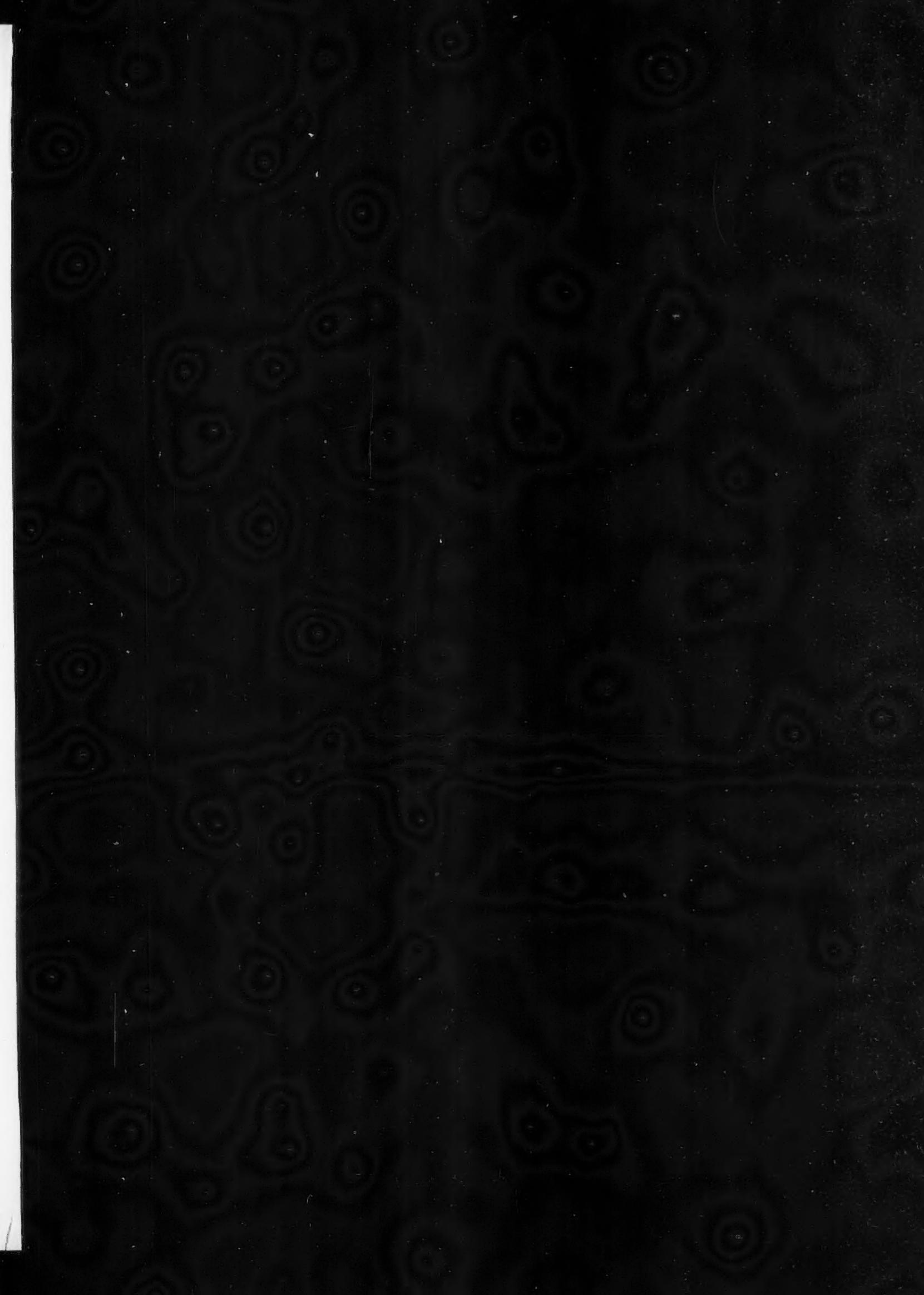
CASE 1.—This 45-year-old Indian woman, M.E., was first admitted to the Vancouver General Hospital on August 14, 1951, with a history dating back to the New Year of 1951, when she complained of a chest cold. Following this she noted tenderness, swelling, and stiffness of the skin of her hands, forearms, knees, ankles, anterior chest and face. The stiffness and induration of the skin later spread to involve the shoulders and trunk. The clinical diagnosis of scleroderma, confirmed by skin biopsy, was made in August 1951. Subsequently she was treated through the years with A.T. 10 (dihydrotachysterol), Priscoline (tolazoline) and other non-specific measures, supplemented by physiotherapy. There was only occasional improvement. Her disease continued to progress, resulting in marked muscular wasting and contracture deformities of all joints of the extremities. By 1955, she had become unable to use her hands (see Figs. 1 and 2) and her skin became "hidebound". Dysphagia and anorexia, with a poor ability to masticate, resulted in a weight loss from 123 to 82 lb. This caused her to be readmitted to hospital in May 1955 for a trial of prednisone (Meticorten) therapy. This was carried out in the Metabolic Unit† of the Vancouver General Hospital.

She was thin and deformed, with a mask-like face and marked restriction of movement of the temporomandibular joints, as well as all joints of the body generally. She had poor chest excursion and slight pitting oedema of both ankles. The skin was smooth and bound down and showed patches of depigmentation. There was marked wasting of subcutaneous tissues and inflexibility of the skin, associated with shortening of distal phalanges of fingers and toes and contractures in flexion and extension of the fingers. Laboratory findings included: haemoglobin value of 9.7 g. %; normal values for serum proteins, with electrophoretic studies showing decreased plasma albumin, slight increase in alpha and beta globulin and marked increase in gamma globulin. X-ray studies revealed general demineralization of bones of the extremities, with loss of the normal cortical structure of hand bones particularly. Barium swallow revealed an area of narrowing and diminished activity of the oesophagus. This was felt to be indicative of sclerodermal involvement of the oesophageal wall. A patchy fibrotic infiltrative process seen in both lungs was further evidence of the systemic involvement.

The patient was started on prednisone (Meticorten) in May 1955, receiving 30 mg. a day. With improvement there was a gradual diminution to a maintenance daily dosage of 10 mg. She made a good clinical response, as judged by her ability to walk, hold a cup and feed herself (see Fig. 3). On prednisone there was no sodium retention or potassium diuresis, her haemoglobin value rose to normal, the sedimentation

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rate diminished and the increased gamma globulin value fell (see Fig. 9). She has been maintained on prednisone 10 mg. daily since her discharge in May 1955, and has gained 17 lb.—from 80 to 97 lb. She has remained ambulatory, with less pain in her hands, and generally has felt better. There was almost no movement in the metacarpophalangeal joints, however. The thumbs were flexed about 20°, and the interphalangeal joints were fixed. On December 2, 1955, while on prednisone therapy, the patient successfully underwent excision of the heads of the fourth and fifth metacarpals of the left hand, with some slight improvement of extension. She was transferred back to a chronic disease hospital on January 26, 1956, where she has been maintained on prednisone (Meticorten) 10 to 15 mg. a day.

The patient was readmitted to the Vancouver General Hospital on January 27, 1957, suffering from a staphylococcal pneumonia. She responded well to penicillin and streptomycin, supported by prednisone, which was increased from 10 to 20 mg. a day to meet the added stress of the acute infection. On recovery she returned to the chronic disease hospital and has been maintained on prednisone 15 mg. a day. The patient has remained ambulatory and is able to feed herself and once again took up knitting, for the first time since the onset of her illness in 1951 (see Fig. 4).

Laboratory studies have been carried out at regular intervals, and as late as November 16, 1957, there was no evidence of electrolyte disturbance or any changes in the fasting blood sugar and serum cholesterol. Present x-ray studies of her chest cage and vertebra compared to those taken in 1955 reveal no apparent change in the density of the bony structures resulting from long-term steroid (prednisone) therapy. The patient's weight on September 23, 1957, was 107½ lb., blood pressure 110/64 mm. Hg; she is very cheerful and attributes her present state of well-being and usefulness to the steroid therapy.

**CASE 2.**—Mrs. M.E., a white woman aged 37, married, was apparently well until 1947, when she developed Raynaud phenomenon of hands and feet, which has persisted. She also has been subject to recurring bouts of severe premenstrual migraine for 15 years. Past illnesses included diphtheria, rickets, appendectomy and the removal of her tonsils and adenoids in childhood. The only other significant information is that she has had three miscarriages. In 1950 she developed what she described as a "cold sore" on her upper lip, which gradually spread to involve her nose, chin and cheek, upper eyelids and right ear lobule, and which did not respond to a variety of topical medications. A biopsy established the diagnosis compatible with the clinical picture of discoid lupus erythematosus. She also showed acrocyanosis.

In 1951, after exposure to the sun, she experienced a flare-up of her rash, associated with facial oedema and accompanied by general malaise, arthralgia, fever, dyspnoea and weakness. She was admitted to the Vancouver General Hospital and laboratory findings were as follows: sedimentation rate 56 mm. in one hr., white cell count 2800, and test for L.E. cells positive. ACTH was given intravenously, with marked clinical and subjective improvement. After discharge



Fig. 1



Fig. 2

Fig. 1 (Case 1).—Generalized scleroderma showing hide-bound effect, mask-like expression and marked weight loss prior to onset of prednisone (Meticorten) therapy. Taken March 1955.

Fig. 2 (Case 1).—Generalized scleroderma showing contracture deformities of hands and depigmentation of skin before prednisone therapy. Taken March 1955.



Fig. 3



Fig. 4

Fig. 3 (Case 1).—Generalized scleroderma showing clinical effects of long-term prednisone therapy. Note weight gain, and ability to feed herself. Taken July 1957.

Fig. 4 (Case 1).—Generalized scleroderma showing beneficial effect in a rehabilitation sense from long-term therapy with prednisone. Taken July 1957.



Fig. 5



Fig. 6

Fig. 5 (Case 2).—Lupus erythematosus disseminatus (systemic) before institution of long-term prednisone therapy and showing activity of her disease. Taken March 1955.

Fig. 6 (Case 2).—Lupus erythematosus disseminatus (systemic) illustrating a very good clinical response to long-term prednisone therapy. Taken July 1957.

from hospital, her disease flared again. Readmissions followed for further courses of ACTH therapy in January, February and June of 1952, with temporary improvement on each occasion. During the remainder of 1952, treatment was limited to bismuth, nicotinic acid, calciferol and atabrine but without success and she remained a very sick person, virtually bedridden.

In January 1953, she was again hospitalized for intravenous ACTH and this was followed up with oral cortisone, 25 mg. 3 times a day, supported by a salt-poor diet and potassium. In January 1954, after a "cold", the patient again became quite ill and was hospitalized; examination revealed an atypical systolic murmur and palpable liver and spleen, plus arthralgias. Once again there was a favourable response to intravenous ACTH, and subsequently she was treated in the outpatient department with cortisone. In March 1955, the patient was readmitted for reassessment preparatory to prednisone (Meticorten) therapy. Despite her taking cortisone orally, 25 mg. 3 times a day, she complained



**Fig. 7 (Case 3).**—Neurodermatitis disseminata showing generalized involvement; note complete alopecia of scalp. Taken March 1955 before onset of prednisone (Meticorten) therapy.

of generalized malaise, arthralgias, and chest pain, in addition to showing activity of her skin lesions (see Fig. 5). The patient was started on Meticorten (30 mg. daily) with marked clinical and subjective improvement, which has been maintained on 15 to 20 mg. of the drug daily. The skin lesions healed, leaving residual scarring and pigmentation (see Fig. 6). Repeated search for L.E. cells has been negative, but she continues to show a high sedimentation rate. Although she fatigues easily, she is no longer bedridden and is able to carry out her household duties. Her blood pressure has remained at 120/70 mm. Hg and there has been no change in electrolytes, blood sugar and cholesterol. X-ray studies have revealed no evidence of osteoporosis over this long-term period of steroid therapy. Since early 1957 she has been troubled by a recurrence of severe premenstrual migraine, associated with anorexia. There has also been a gradual weight loss of 18 lb. over this period, which may in part be due to the catabolic effect of prednisone (compare Figs. 5 and 6).

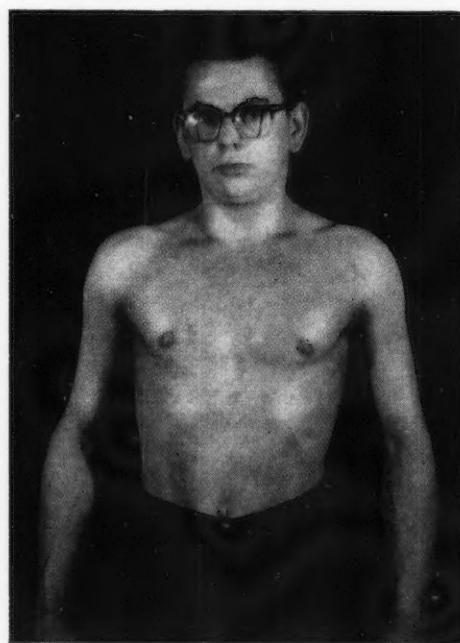
**CASE 3.**—The patient, J.W., a white male, single, aged 18 years, presented with a long history of atopy, having had infantile eczema and asthma in childhood and neurodermatitis disseminata during adolescence. Two years before the present admission the neurodermatitis disseminata flared up and became generalized, resulting in a completely incapacitating exfoliative dermatitis which had confined him to bed for an entire year.

Upon admission to hospital on March 3, 1955, the patient was in an acute state of depression. He lay curled up in bed in the flexed fetal position. He was buried under the sheets and showed extreme sensitivity to the slightest temperature change. The entire skin surface was reddened, oedematous and scaly, with extensive exudative areas. This was associated with complete alopecia of the scalp and with secondary pyoderma (see Fig. 7).

The admission weight was 106 lb. Temperature was 100° F., and the pulse was regular at 120. The physical examination showed no pathological features other than those already described. The haematocrit was 45. The white cell count was 7950, with 19% neutrophils, 26% band cells, 20% lymphocytes, 6% monocytes, 26% eosinophils, and 3% basophils. The circulating eosinophils were 1755 per c.mm. The sedimentation rate was 20 (Winrobe method). The blood sugar was 80 mg. fasting. Cholesterol 180 mg., non-protein nitrogen (NPN) 16 mg. Blood protein 5.5, with an

albumin-globulin ratio of 2.8-2.7. The electrolyte level was Na 147 mEq./litre, K-4.7, chloride 109 and the  $\text{CO}_2$  combining power 32.

**Treatment.**—He was treated initially with intravenous ACTH for one week with spectacular improvement, but this was not maintained with intramuscular ACTH (Duracton) in the dosage used. On March 19, 1955, the ACTH was replaced by prednisone (Meticorten), a total of 30 mg. daily. This dosage was increased to 40 mg. daily in order to obtain a maximal clinical response with a complete involution of the oedematous, exudative and erythematous phase. The patient has been maintained continuously on prednisone for two and one-half years, the dosage varying from the initial 40 mg. daily to 10 mg. daily during the induced remissions. Upon discharge from hospital on April 4, 1955, he was able to hold a full-time job and to lead a normal active life, although the skin continued to show some erythema with residual lichenification and pigmentation. There has been a complete regrowth of hair since the prednisone therapy. In November 1955, he was readmitted to hospital for clinical evaluation. He had gained 10 lb. in weight. The skin remained clear. The blood chemistry showed no change. The adrenal glands were markedly depressed, as evidenced by a lack of fall in eosinophil count following ACTH given as an intravenous drip, eight hours daily for five days. This depression has been described by many workers<sup>4</sup> and is considered to be temporary and reversible. The patient was therefore discharged from hospital on continued prednisone. On March 10, 1956, after a short respiratory infection he was brought to the emergency department in acute collapse—not unlike an Addisonian crisis. The pulse rose to 150 and was irregular and almost imperceptible. His blood pressure fell to 65 mm. Hg systolic. His heart became acutely dilated, his lungs engorged, and the urine was packed with red blood cells. Intravenous hydrocortone proved to be a life-saving measure and its use was accompanied by antibiotics in massive doses. On June 23, 1956, after



**Fig. 8 (Case 3).**—Neurodermatitis disseminata showing favourable clinical response to long-term prednisone therapy; note complete regrowth of hair.

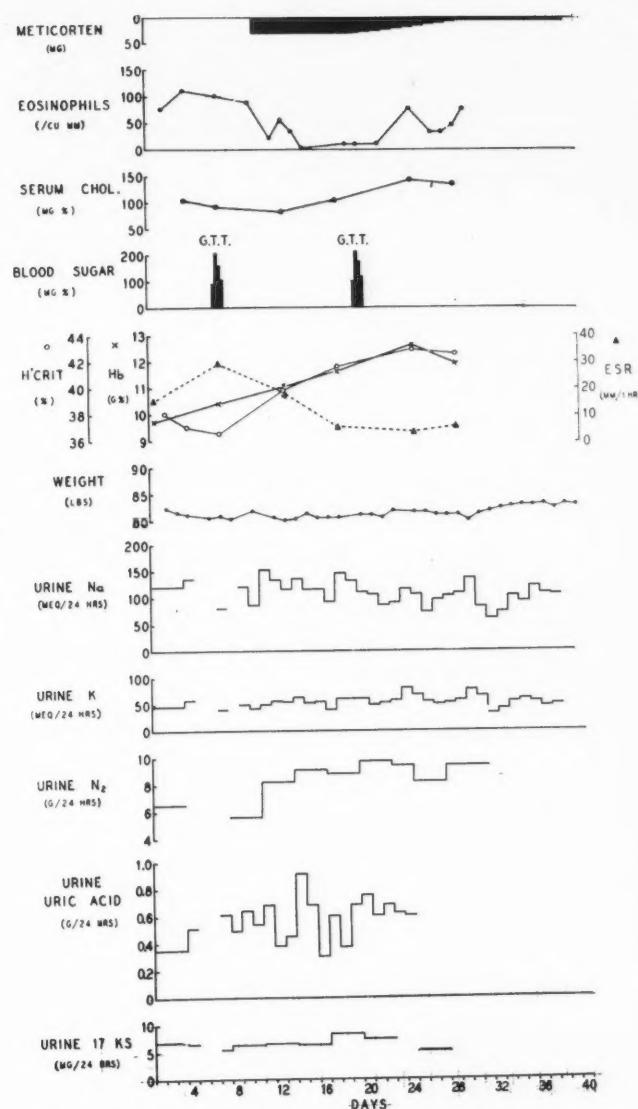


Fig. 9.—Laboratory investigations and findings on Case 1 (generalized scleroderma) at the outset of prednisone (Meticorten) therapy.

a rather severe flare of the skin, another attempt was made to stimulate the patient's adrenals with intravenous ACTH. This attempt was abandoned after one week, both because of lack of fall in circulating eosinophils and a poor clinical response. In November 1956, he developed furunculosis, having as many as 50 boils at one time. These failed to show the usual erythema, were very poorly localized, and had little tendency to point. At no time was there an accompanying febrile reaction. Upon incision, large amounts of purulent material were expressed which contained colonies of staphylococci on direct smear. These organisms were at first sensitive to chloramphenicol, novobiocin and erythromycin, but later became insensitive to all the usual antibiotics. The furunculosis became a very serious problem requiring hospitalization almost continuously from November 1956 to May 1957. The boils improved when massive antibiotics were given along with prednisone (Meticorten) but invariably recurred as soon as the antibiotics were stopped. In February 1957, the infection was considered to be of greater danger than the accompanying dermatitis, and it was thought to be impossible to control it as long as the patient received steroids. It was, therefore, attempted to withdraw the steroid after

very gradual reduction in dosage. As soon as the prednisone was discontinued the patient rapidly regressed to his original state. With full cognizance of the risks involved and after a course of intravenous Vancomycin, the patient was put back on prednisone. He has been carried since May 1957, with no antibiotics and with no recurrence of boils, and is able to maintain full-time employment while on a dose of prednisone, 12½-15 mg. daily (see Fig. 8).

#### CLINICAL LABORATORY FINDINGS\*

The most complete laboratory investigation was undertaken on the patient M.E. (see Fig. 9). After institution of therapy there was a gradual fall in the number of circulating eosinophils and in the erythrocyte sedimentation rate. The decrease in circulating eosinophils was maintained during the period of high dosage but was not sustained when the dose was reduced. There were no laboratory evidences of retention of either water or electrolytes, and the body weight remained stationary. However, there was a definite increase in haemoglobin concentration, hematocrit reading and urinary nitrogen excretion. Nitrogen balance studies were not undertaken, but others<sup>2</sup> have reported that no change occurs during the administration of prednisone to patients on liberal diets. The findings, including the nitrogen excretion, in this patient may be explained by the increased ingestion of food resulting from the improvement in deglutition and her ability to feed herself during therapy. Contrary to the findings of others,<sup>2, 4</sup> there was no

\*Dr. John Eden, chemical pathologist, Vancouver General Hospital, lent his assistance in interpreting the above laboratory findings.

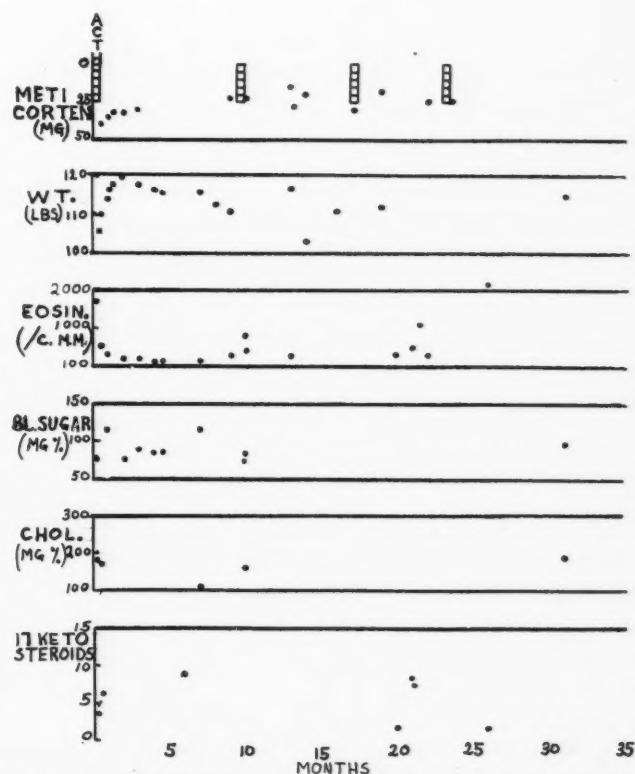


Fig. 10.—Laboratory data during two and a half years of therapy with prednisone (Meticorten) in Case 3—generalized neurodermatitis disseminata.

change in the 17-ketosteroid excretion. Increases in serum cholesterol concentration have been reported during the administration of prednisone and a minor increase from low<sup>2</sup> to high normal levels was demonstrated in this patient. No change occurred in the glucose tolerance test.

The laboratory and clinical findings support the claim that prednisone is more effective than cortisone, and in the dosage required it does not possess sodium-retaining properties.

#### DISCUSSION

The above three patients have been maintained on continuous prednisone (Meticorten) therapy in dosage varying from 10 mg. to 40 mg. daily for a period of two and a half years. There has at no time been any clinical or laboratory evidence of electrolyte imbalance. There has been no change in blood sugar, cholesterol and NPN. These observations are similar to those of Cohen *et al.*<sup>5</sup> in their long-term use of prednisone in rheumatoid arthritis. In one case (Case 3) in which 17-ketosteroid values were followed during this entire study there was a very marked fall in the 17-ketosteroids to 1.6 and 1.7 in 24 hours (see Fig. 10), as has been demonstrated previously by others.<sup>2, 4</sup>

A serious complication, noted by others<sup>6, 7</sup> and which we encountered during this period, was the development of staphylococcal infection, as evidenced by pneumonia in two patients, one of whom subsequently developed troublesome generalized furunculosis which required hospitalization. Both showed a favourable response to specific antibiotics while being maintained on increased dosage of adrenocortical steroids.

In Case 1 it was found sufficient merely to increase the daily dose of prednisone, but in Case 3 the staphylococcal infection appeared to be overwhelming and the clinical picture was one of complete circulatory collapse and near death from adrenal failure. The adrenals, being markedly depressed from long-term treatment with prednisone, failed to respond to the sudden increased need for cortical hormones accompanying an acute overwhelming infection. This is probably the most serious hazard of long-term steroid therapy. It must always be borne in mind that in times of stress, such as infection or surgery, the body normally responds by a tremendous increase in the production of adrenal corticoids. The steroid-treated patient is incapable of making such a response. Therefore, the hormone must be supplied from without in increased dosage and in a rapidly available form, the best probably being intravenous hydrocortisone. It is entirely useless under these circumstances to use ACTH, for the latter can only act by stimulating the adrenal to produce its own corticoids. The severely depressed adrenal cannot make such a response and therefore ACTH is completely ineffectual. Subsequently these two patients have been able to continue their prednisone (without antibiotics), and have remained free

from staphylococcal infection to date. We have not observed gastric complications in these cases.

The clinical response to prednisone in these three patients has been most striking, when one considers that all three were completely incapacitated and virtually bedridden before steroid therapy. On prednisone the patient in Case 3 has been able to return to full-time employment and has had a complete regrowth of hair on his scalp. The second patient can now do her household duties, and the first is able to get out of bed without help, to feed herself, and has sufficient use of her hands and fingers to knit (see Fig. 4). In the past year, the second patient has shown evidence of the catabolic effect of steroid therapy by considerable weight loss. To date these patients have been maintained in a state of well-being on long-term prednisone therapy which remains as effective now as it was initially. But as yet we have been unable to withdraw the drug, and this is in keeping with the observations of Robinson.<sup>10</sup>

#### CONCLUSIONS

Long-term therapy with prednisone (Meticorten) in systemic lupus erythematosus, generalized systemic scleroderma, and generalized neurodermatitis disseminata was shown to be feasible and appears to be justifiable in these seriously disabling diseases.

One of the major risks of long-term steroid therapy is a lowering of resistance to bacterial infections, particularly *Staphylococcus aureus*. When acute infection supervenes, it is important to increase the dosage of corticosteroids immediately and to cover with specific antibiotics. ACTH should not be substituted during times of increased stress.

A patient with lupus erythematosus disseminatus (systemic) on long-term prednisone therapy is showing a weight loss which may be due to a catabolic effect of the hormone.

No disturbance of serum electrolytes, blood sugar, cholesterol, non-protein nitrogen or blood pressure has followed long-term prednisone therapy in dosage used.

Appreciation is expressed to Miss K. Hoskins of the Photography Department of the Vancouver General Hospital and to Mr. Fred Herzog of the Photography Department of St. Paul's Hospital for the illustrations.

Prednisone (Meticorten) used in these cases was generously supplied by Dr. W. K. MacDonald of the Schering Company, Montreal.

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## CLINICAL OBSERVATIONS OF SUICIDE

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THE PROBLEM of estimating suicidal intention and obviating the suicidal act remains a difficult challenge. However, it is a daily task for the psychiatrist who must evaluate and assess the forces at work in patients who are suicidal risks. The evaluation is more critical, the penalty of error more obvious, when one deals with suicidal patients in office practice, since there the controls and protection of a hospital environment are not part of the therapeutic program. The purpose of this paper is to present and discuss data gathered from personal experience with 33 patients who, while in psychotherapy or shortly after being examined, attempted suicide. For nine patients, it was a successful attempt.

Certain aspects of the suicide problem have been reported and discussed and are generally agreed upon, but as Bellak<sup>1</sup> has noted, there is still not a great deal known about the basic facts even in cases of clinically overt suicide. Raines<sup>2</sup> has pointed out that suicide is the leading cause of death in psychiatry, except in the oldest age group. Statistics regarding suicide are difficult to assess, since an unknown number are not reported, and others are overlooked in the concealed suicides which occur through accidents, or in the physiological suicide through alcohol or drug addiction, or in the neglect of obvious and urgently recommended health precautions. Raines reported that in a "normal" group questioned, suicidal ideas were admitted as "passing thoughts" in over half of the group. The suicidal ruminations of an obsessive character are much more indicative of a disturbed psychopathology, but the precise relationship of such ruminations to attempted suicide is actually not clear. Whatever one may think about statistics and their accuracy, it must be generally accepted that the suicidal attempt is the most common emergency with which the psychiatrist is called upon to deal.

Zilboorg<sup>3, 4</sup> has discussed some of the common misconceptions about suicide and described the act as an archaic response to inner conflicts and by no means restricted to the patient diagnosed as suffering from depression. This is generally agreed to by most psychiatrists who can record the attempt in patients carrying a variety of diagnostic labels, including depression, schizophrenia, psychopathic state, character neurosis and others.

Several authors<sup>5-8</sup> have reported on the close association between the suicidal patient and mental illness, and the high incidence of familial mental disorder in such cases. There are a number of

reports dealing with patients who have been studied in general hospitals after attempting suicide. These authors report approximately similar clinical findings, but express divergent interpretations of these findings and different views regarding subsequent management and disposal. Ettlinger and Flordh<sup>9</sup> have reported their experience in a general hospital with 500 cases of attempted suicide. Most patients had histories of mental symptoms and previous psychiatric treatment, and 29% had made previous suicidal attempts. Precipitating factors were recorded to be alcohol, worry, loss of work and other reality stresses. Disposal was so carried out that 52% of these patients were admitted to the psychiatric wards and 30% to medical wards, and the remainder were discharged to their homes. They concluded that the suicidal attempt is symptomatic of mental imbalance, and that this large number of suicidal patients underlined the need for expanded psychiatric facilities. A similar study was reported by Batchelor and Napier,<sup>10</sup> but less than one-third of 200 patients in their series required mental hospital care and 57% were immediately sent home. The mortality in their series after one year was just over 10%, as a number of discharged patients had by then successfully committed suicide, and a few others had repeated their previous attempts. They concluded that this justified a rather free disposal policy. A similar point of view was expressed by Offenkrantz, Church and Elliott,<sup>11</sup> in reporting on the management of threats of suicide amongst military personnel. In this selected group, where secondary gain is so obvious, they felt that firmness and refusal to yield to "emotional blackmail" served as a useful technique in meeting this problem. It should be emphasized at this point that the suicidal gesture is far different in meaning from the urgent suicidal threat. In a paper on attempted suicide among veterans, Simon's<sup>12</sup> findings were more consistent with other reports on non-military groups. Most of these veterans were ill with depressions, schizophrenia and other severely disturbed mental states, with an average illness duration of 13 months before the reported attempt. The implication here is rather that suicide is a serious matter and associated with a grave emotional disorder. Levy and Southcombe<sup>13</sup> also share this view, in pointing out that the suicide rate is much higher in a state hospital than it is for the general population. This obviously relates to the greater concentration of sick people in hospital, but also suggests the interesting fact that hospitalization is not a complete protection to ward off suicidal attempts, no matter how far precautions may be taken.

Publications dealing with events that precipitate a suicidal attempt outline familiar factors that usually contribute to a depressive illness. Here the interaction between the external event and the impact on the vulnerable personality is usually stressed. Kirboe<sup>14</sup> studied suicide among a group

\*Presented at the Quebec Provincial Psychiatric Association Meeting March 7th, 1958.

of old people and outlined the main precipitants as pain, chronic illness, somatic inconveniences, depression. He also noted a high incidence of alcoholism and syphilis in his group. Eidelman<sup>15</sup> noted that sickness, disability, the death of relatives or frustrated love affairs were precipitants particularly in depressed hysterical patients. A reliable danger signal was found to be the depth of hostility in the patient to someone close, and it was this author's recommendation that hospitalization is the most effective form of protection against suicide. Sisler<sup>16</sup> concluded also that all persons who attempt suicide should be admitted to a hospital with psychiatric facilities and be retained long enough to have a thorough psychiatric assessment. "The suicidal attempt is a symptom of many different psychopathologic and social conditions, and the specific therapy of the suicidal patient involves the treatment of these conditions."

Any therapist dealing with the suicidal patient is well aware of the impact on the family and surrounding constellation, but, rather strangely, this aspect of the problem has received scant attention. Perhaps the anxiety stirred up involves the psychiatrist to share the "conspiracy" of silence. Stengel<sup>17</sup> studied this aspect of the case history of 138 patients, and found that for many patients the suicidal attempt crystallized certain conflicts of the individual with his environment and led either to a cementing or to a frank rupture of precarious relationships.

The meaning and motivation of the suicidal wish, gesture, attempt or final act is most thoroughly documented by Menninger<sup>18</sup> in "Man Against Himself". He describes the three components of the suicidal act as: (1) the desire to kill (someone else), (2) the desire to be killed, and (3) the wish to die. He describes the suicidal act as a murder of the self by the self and points out that it is a special kind of death in which there are combined in the one person the murderer and the murderer. However, no suicide is consummated unless, in addition, the suicidal person also wishes to die. These components involve and express different aims. The wish to kill is derived from primitive aggressions aroused by thwarting and no longer successfully redirected, displaced and sublimated by love or other constructive forces. The suicide's motive is often the murder of the hated introjected object. Just as killing is the extreme of aggression, so is being killed the extreme form of masochistic fulfilment. The submission, defeat and pain ending in death itself is an unconsciously directed aim, serving the command of the sadistic superego. The conflict between these opposing aims is best seen in those patients who are showing clinical improvement as they begin to emerge from a psychotic depression and begin to give expression to hostile emotions so long repressed. This is especially a time when suicide is prone to occur. Freud<sup>19</sup> long ago stated that "many suicides are disguised murders". The

wish to die is described as an expression, mainly oral, of hopes for passive gratification, achieved through the reunion with or identification with someone who is the mother object. Fenichel<sup>20</sup> stated that:

"The suicide of the depressed patient is, if examined from the standpoint of the superego, a turning of sadism against the person himself, and the thesis that nobody kills himself who had not intended to kill someone else is proved by the depressive suicide. Other suicidal acts assert themselves as desperate attempts to enforce, at any cost, the cessation of pressure of the superego. They are the most extreme acts of ingratiatory submission to punishment and to the superego's cruelty; simultaneously they are also the most extreme acts of rebellion, that is murder-murder of the original objects whose incorporation created the superego."

"Suicide is carried out because hopes and illusions of a relaxing gratification are connected with the idea of suicide. What is often striven for in suicidal attempts is not the destruction of the ego, but some libidinous aim, which through displacement has become attached to ideas which objectively bring self-destruction—such as the hope of joining a dead person, a libidinous identification with a dear person, the oceanic longing for a union with the mother or even simply orgasm itself."

Moll<sup>21</sup> has discussed various meanings and attitudes about death in considering the psychopathology of suicide. He found that some suicide phantasies are aimed at injuring society or someone close and also represent unconscious death wishes; in others, the phantasies are compelling forces to extract increased love or punishment; in still others, the suicidal phantasies bring the perfect union with an ideal unobtainable in life. "Suicide should not be considered as just an act or an isolated occurrence, but as a culmination of conscious and unconscious events which in all their aspects results in a person's faulty adaptation to life."

#### CLINICAL CASE MATERIAL

I imagine that my own experience is similar to that of many other psychiatrists who are engaged in private practice and are also attending at either general or psychiatric hospitals. The suicidal threat or actual attempt is frequently the crisis which leads to the initial psychiatric examination and brings the mobilization of various therapeutic resources into the situation. The patient less obviously motivated towards suicide is equally familiar. This includes the alcoholic, the drug addict, the person who constantly flirts with disaster, the obsessional who works himself towards death if not to death, the organically sick patient who denies the illness and neglects the coronary impairment, the surgical addict and the accident prone, amongst others. Patients in psychotherapy often recall phantasies of suicide during childhood,

TABLE I.—UNSUCCESSFUL ATTEMPTS AT SUICIDE

<i>Age</i>	<i>Sex</i>	<i>Marital status</i>	<i>Diagnosis</i>	<i>Method of suicide</i>	<i>Comments</i>
1 33	F.	M.	Character neurosis depression	Barbiturates	Intermittent psychotherapy with improvement.
2 54	F.	M.	Paranoid depression	Barbiturates	Discontinued psychotherapy.
3 48	F.	M.	Schizo-affective	Barbiturates	Psychotherapy with improvement.
4 52	F.	M.	Character neurosis depression	Barbiturates and wrist slashing	Commitment.
5 30	F.	M.	Schizo-affective	Barbiturates and wrist slashing	Frequent commitments, lobotomy, improved.
6 26	M.	S.	Schizo-affective	Drowning	Psychotherapy, improved.
7 24	F.	S.	Schizophrenia	Barbiturates	Psychotherapy, improved.
8 65	M.	M.	Involutional depression	Barbiturates	Hospital with electroconvulsive therapy (E.C.T.), recovered.
9 29	F.	M.	Schizo-affective	Barbiturates	Psychotherapy, improved.
10 56	F.	W.	Schizo-affective	Barbiturates and gas	Commitment.
11 43	F.	M.	Acquired epilepsy and reactive depression	Barbiturates	Psychotherapy, improved.
12 65	F.	M.	Involutional depression	Barbiturates	E.C.T., recovered.
13 42	M.	M.	Manic-depressive (circular)	Barbiturates	Psychotherapy, improved.
14 47	M.	M.	Schizo-affective	Hanging	E.C.T. with psychotherapy, improved.
15 36	F.	S.	Schizophrenia	Barbiturates	Psychotherapy, improved.
16 37	F.	S.	Schizophrenia	Barbiturates and wrist slashing.	Repeated commitments.
17 53	F.	M.	Involutional depression	Barbiturates	Refused treatment, later committed.
18 29	F.	D.	Schizo-affective	Barbiturates	E.C.T., refused psychotherapy.
19 40	M.	M.	Schizophrenia	Barbiturates	Refused treatment.
20 21	F.	S.	Schizo-affective	Barbiturates	Psychotherapy, improved.
21 19	F.	S.	Schizo-affective	Barbiturates	Psychotherapy, improved.
22 47	F.	M.	Depression	Barbiturates	E.C.T., refused psychotherapy.
23 43	F.	M.	Depression	Barbiturates	E.C.T. plus hospitalization. Short-term psychotherapy with improvement.
24 42	F.	M.	Reactive depression	Barbiturates	Refused psychotherapy.

and these usually represent an attempt at mastery of a hostile environment. Typically, in such fantasies, the person visualizes his own funeral, while the parents are punished by grief, devastated by their loss and tormented with guilt for not showing greater love and devotion. More urgent suicidal wishes are less often recalled from childhood, and occasionally abortive suicidal gestures that were acted out. Still considering the field of feeling and phantasy, obsessional ruminations do occur in depressed and agitated patients of any age, and are seen in phobic states and in many other clinical states of ego disorganization. A word should be added here about the fears of death or insanity, which are so common in acute conflict. Actually each idea contains the denial and the wish. The patient is presented with alternative solutions to his conflict, but neither is wholly acceptable. The fear of insanity is often associated with the less conscious wish for the free emergence of the instinctual strivings. The fear of death represents the reaction formation to the wish for death—a death conceived as a state of fulfilment, a state of passive gratification and freedom from struggle and psychic pain.

Actually, a very large number of patients have come to my attention after a suicidal attempt, but these have been purposely excluded from the present data, in the effort to minimize the inevitable distortions which arise in trying to reconstruct and understand the act after the fact. The present material is restricted to the con-

sideration of 33 patients, all of whom were either in psychotherapy or who were at least examined and evaluated before the suicidal attempt. I believe this permits a more reliable clinical observation, and allows for a fuller and more dynamic recognition of the patient's interactions within his family and among his friends and acquaintances. Of this total of 33 patients, 9 patients succeeded in their attempt.

#### UNSUCCESSFUL SUICIDES

This group of 24 patients consists of 18 women and 6 men. The age range varied from 19 to 65, with most falling in the 35 to 45 year range. The method used in 22 patients was barbiturate overdosage, with additional wrist slashing in two patients and bathtub drowning and gas poisoning in two others. In this group, nine patients had started therapy briefly but had discontinued against advice; within a short time, the suicidal attempt took place, followed by the resumption of therapy in some cases. Nine of these patients afterwards carried on in psychotherapy for a varying period and did very well. Seven patients received electro-shock along with other emergency treatment measures, e.g. hospitalization in some cases. Four refused any therapy and subsequently were committed after further deterioration of their health or a renewed suicidal attempt. One patient who had attempted suicide repeatedly during the history of schizo-affective psychosis was uninfluenced by

any therapy until a lobotomy was performed two years ago; she has been symptomatically well since then. Of the total group, 13 patients were diagnosed as schizophrenic or schizo-affective psychotics, nine were diagnosed as severely depressed, one as circular manic depressive, and one as suffering from acquired epilepsy with a reactive depression. An outstanding feature in the history of these patients was the fact that in 10 cases the mother of the patient was currently overtly psychotic, or had been in the past; and in an additional 10 others, the parent most significant to the patient's superego formation and intrapsychic conflicts had been grossly emotionally ill, if not psychotic. Of the 16 patients who were married, all had ambivalent and highly unsatisfactory relationships to their mates. The situation leading to the suicidal act most often involved a violent struggle with a key figure in the patient's illness, associated with a storm of guilt and fears of abandonment.

**CASE 1.**—Married woman of 33. Obsessional character neurosis with severe depression. Disturbed marital relationship. Hysterectomized and childless. Psychotic mother separated from a long absent father. Had started psychotherapy for about three months. The physician who was taking care of the psychotic mother telephoned this patient and advised her to be more thoughtful and considerate of her mother, etc. This was followed by ingestion of a large dose of barbiturates. After recovery, this patient never saw her mother or spoke to her again, considering the separation between them as now final and complete. She had follow-up psychotherapy and has done well clinically.

**CASE 5.**—Single woman of 36. Schizo-affective disorder. She had spent all her adolescence and adult years caring for a psychotic mother who was kept at home at the insistence of the other family members. Finally matters became so unbearable for all that the mother was committed to an institution. The patient experienced extreme guilt, and very shortly after her mother's removal, and about two months after her own therapy started, attempted suicide with barbiturates. She notified me before coma set in. Since then, the patient has referred to this experience as "Do you remember when I committed suicide?" The expiation of her guilt, the psychic separation from her mother, the mobilization of the family to her side after punishing them, and the forgiveness and support of the omnipotent therapist were all achieved in the one act. With follow-up psychotherapy, she has reached a surprisingly good adjustment.

**CASE 8.**—Married woman of 29. Schizo-affective disorder. Disturbed marital relationship. Psychotic mother who had been through hospitalizations, lobotomy and many other procedures without benefit. Patient started in therapy about five months before her own attempt. Her mother at this time attempted suicide with barbiturates and gas. After two weeks of uncertainty, her mother's survival was assured though she was left with a permanent paraplegia induced by brain damage from carbon monoxide. When it became clear that her mother's recovery was definite, the patient herself

attempted suicide with barbiturates. She telephoned me before losing consciousness and was resuscitated. With follow-up psychotherapy, she has achieved a much improved life adjustment.

**CASE 16.**—Divorced woman of 29. Schizo-affective disorder—completely dependent upon and manipulated by a psychotic mother in a "folie à deux". Patient started therapy and began attempts to free herself from her mother's influence. After about one month, an intense quarrel with her mother took place, and the patient ingested a large dose of barbiturates. She was revived, but her mother would not allow her to continue in therapy.

**CASE 23.**—Single woman of 21. Schizo-affective disorder. A rejected and over-protected only child of wealthy parents, locked all her life in a continuous struggle with an obsessional sadistic father. Her symptoms were states of alternating obesity, depressions and transient disorganized hallucinated states. During the first months of therapy, she began to move towards greater psychic freedom. After a particularly hostile burst from her father, she took a large dose of barbiturates and just before coma set in, she told her mother, "This is what Daddy would want." She was resuscitated and she continued in therapy with considerable improvement. After a great deal of manoeuvring she has managed to live away from her parents.

In considering the case material of these unsuccessful suicides, a number of impressions stand out clearly. First of all, one can say without reservation that these patients were very ill psychologically. However, hope did remain within them, as attested by their undertaking treatment. Of the more obvious motivations determining the suicidal attempt, the main factors were feelings of revenge and uncontrollable hatred towards a needed person, associated with marked guilt feelings. The desire to die seems to have been truly absent in these patients, or present in a minimal degree. As noted in the brief case outlines, the patients notified me or someone else they could trust after a determined suicidal attempt was made. It should be noted that these cases involved serious attempts, not gestures. All required stomach lavage and life-saving measures. I have the impression that the transference relationship in these patients was an additional and potent factor in their persisting interest in life and survival. It is also true that the conflicts emerging more sharply in the process of treatment itself can at times determine the time and give a meaning to the suicidal act, as an expression of and an acting out of transference emotions.

**CASE 1.**—Married man of 52. Severe agitated depression with history of two previous depressions. Diagnosed manic-depressive depression. A passive, dependent, unsuccessful man dominated by an aggressive controlling wife, who critically and loudly called attention to his shortcomings as a man. Immediate hospitalization was urgently advised as suicidal ruminations were insistent. The patient's wife refused her consent and disregarded the advice regarding the dangers. Three days later, the man hanged himself.

CASE 2.—Married woman of 38. Schizo-affective disorder. A lifelong passive dependent hostile relationship to a paranoid prepsychotic mother from whom she could obtain support only by helpless submissiveness. A striking pattern of illness and surgery began in adolescence as a technique of dealing with her own needs and reacting masochistically to a cold hostile environment. Polysurgical addiction included tonsillectomy, appendectomy, bilateral mastectomy, removal of intervertebral disc, spinal fusion (two operations), plastic surgery. All of these procedures were done on elective grounds and in the face of divided medical opinions. Married to a schizoid man who was completely inadequate to deal with her insatiable infantile demands. She started psychotherapy when deeply depressed, after a suicidal attempt with resuscitation at a general hospital. After a short period of therapy, she was institutionalized for three months and did very well removed from the hostile environment. When she resumed therapy there was an unusual amount of interference from her mother when a very weak transference relationship developed—always in jeopardy because of insatiable needs for support. She was addicted to drugs which she obtained by visiting a variety of doctors. Her husband was issued paraldehyde to administer as directed and duly warned regarding suicidal risks. He promptly turned the whole bottle over to the patient and went out for the evening. She took an overdose and was revived with difficulty. At this point, I insisted on readmitting her to hospital but her mother was adamant in refusing, declaring she would rather see her dead than in an institution. At this point, I advised another therapist and withdrew from the case. She was under treatment fitfully with another therapist for about six months, when, after another quarrel with husband, she committed suicide with barbiturates and monoxide poisoning in the closed garage. Her husband slept through the night and discovered the body in the morning.

CASE 3.—Married woman of 50 suffering from paranoid depression. Her first visit was ostensibly motivated by the desire to get a certificate of mental fitness, so that her will would not be challenged. She detailed a well-developed delusional system regarding her husband's infidelity, with gross psychotic distortions. This had become marked following a mastectomy to which she reacted as if it was a disfiguring castration. The second visit confirmed the clinical impression of severe depressive elements which prognostically gave considerable hope of response to treatment. Exploration established her unwillingness to co-operate, as denial was a primary form of defence. Her husband was called in, and the suicidal risk was sharply drawn, along with the urgent recommendation for commitment. He refused to consider this, and expressed a long-suffering hopelessness in his marital relations. He described his mother-in-law as having had a similar disorder. He "would rather see her dead". The patient committed suicide about six weeks later by the ingestion of a large amount of barbiturates and by gas poisoning in a rented room.

CASE 4.—Divorced woman of 38 with a circular manic-depressive psychosis. Although committed on many occasions for manic excitements she suffered also from severe depressions which had escaped special notice or treatment. She was away from home, working

as a nursery school teacher, and living in a rented room. She presented herself in a severe depression with suicidal ideas after an unsuccessful attempt at reconciliation with her husband. The family with which she was living were to be away and leave her alone for four days. Her family was contacted, with a view to rehospitalizing her, as she was severely ill and suicidal. They showed only a hostile reaction to her very existence. She took her life over this week-end, using barbiturates and gas poisoning.

CASE 5.—Married man of 53. Severe involutional depression in an obsessive man, extremely dependent upon his wife in a childless marriage. Acute conflict had arisen out of their foster adoption of an adolescent D.P. boy to whom his wife had become excessively devoted. The patient expressed suicidal ruminations. Immediate hospitalization was recommended, attention being drawn to the urgent suicidal risk. She was non-committal about the whole matter. On a subsequent week-end she took a trip out of town for three days, leaving the patient alone during this period. He committed suicide with barbiturates and gas.

CASE 6.—Married female of 47. Manic-depressive circular with marked paranoid traits. Her mother had killed herself by jumping from a height when patient was six years old. Patient had always felt bitter and abandoned, and had a constant feeling of deprivation, emotional and financial, with severe distortions of reality. There was a markedly hostile relationship to her husband, who was essentially passive and ingratiating, but stooped to various deceptions to avoid her storms of temper. The patient had been hospitalized several times with no benefit. I recommended her commitment on my first examination because of a severe and agitated depression with suicidal ruminations. She did well and left hospital after several months. The therapeutic contact could not be maintained as she refused to become involved, feeling that nothing could be done. Another recurrence of depression led to her readmission to hospital, this time by the certificate of another psychiatrist. The patient was apparently improving after a stay in hospital and was moved to an open ward. On a week-end visit from her husband, she asked him whether or not she might return for treatment with me after discharge. He was hostile and discouraging, telling her I was just as fed up with her as he was, because she was so unreasonable. Several days later, the patient eloped from hospital, came unannounced to my tenth floor waiting room and, without asking to see me, jumped to her death from the window.

CASE 7.—Single man of 29. Schizo-affective psychosis. A college-educated older son of a professional man. Both parents were psychologically disturbed. A younger brother was much more aggressive and successful socially. A feeble attempt to pursue a desirable young woman failed and he deteriorated rapidly into a depressed apathetic state, with self-accusatory ruminations and an increasing awareness of passive homosexual strivings. His parents were advised of the urgencies of the situation and his commitment was recommended. They decided to wait for admission to a socially more desirable institution, meanwhile voicing their pessimism about any chances for recovery. The patient obtained a gun and shot himself through the

TABLE II.—SUCCESSFUL SUICIDES

<i>Age</i>	<i>Sex</i>	<i>Marital status</i>	<i>Diagnosis</i>	<i>Method</i>	<i>Comments</i>
1 52	M.	M.	Manic-depressive (depression)	Hanging	Relatives refused commitment.
2 38	F.	M.	Schizo-affective	Barbiturates and gas	Relatives refused commitment.
3 50	F.	M.	Paranoid depression	Barbiturates and gas	Relatives refused commitment.
4 38	F. Separated		Manic-depression (circular)	Barbiturates and gas	Relatives refused commitment.
5 53	M.	M.	Involutional depression	Barbiturates and gas	Relatives refused commitment.
6 47	F.	M.	Manic-depression (circular)	Jumped from height	Eloped from hospital to suicide.
7 29	M.	S.	Schizo-affective	Gunshot	Relatives refused commitment.
8 27	M.	M.	Manic-depression (circular)	Barbiturates	Relatives refused commitment.
9 41	M.	M.	Manic-depressive (depression)	Train	Awaiting hospitalization.

head while his parents were out. He had neatly spread towels about him to avoid making a mess in the room.

CASE 8.—Married man of 27. Manic-depressive circular. The older son of an obsessive socially prominent successful father, always a disappointment to his father and since childhood locked in a ceaseless ambivalent struggle to earn his father's love, and to rebel against and overwhelm him at the same time. He had been in psychiatric treatment since childhood—with the same result, always the psychotherapist had been drawn into the untenable position of refereeing the struggle between son and father. The mother was a chronically depressed hostile woman, submissive to her husband's dictates. The patient had been institutionalized on several occasions, usually for manic episodes, when he signed cheques and started the kind of spree which would socially embarrass his father. Within a short time after starting therapy with me, he decided to marry a chorus girl, thus outraging his father. In the skirmishes around this matter, the patient attempted suicide with barbiturates and was revived. His depressed and suicidal ruminations persisted. The family at this point was urged that he be recommitted. The father refused, claiming that the patient was merely using gestures, faking, and finally declaring he did not care what happened anyway. I was adamant about the advice being taken. This resulted in a termination of my contact with the patient. The patient married the girl, was rejected by the family and about four months later, took a lethal dose of barbiturates in a hotel room.

CASE 9.—Married woman of 41. Manic-depressive depression. Hysterectomized. The depression was not evident but her main complaints were of a somatic nature. The patient denied any suicidal ruminations, but arrangements were made for her admission to hospital for further observation. Several days later, the patient committed suicide by throwing herself in front of a train. The husband could not understand this happening, as there had been no inkling and no warning of impending disaster. The clinical evaluation here was regarded as incomplete and unsatisfactory.

Two patients in this group of nine had been seen by the author once, and another patient twice. The remainder were in treatment for periods varying from a few to many months. The last case, in which suicide was not really anticipated, serves as a timely reminder for constant awareness. In the other eight cases, not only was suicide recognized by the author as a serious threat, but steps were initiated to obviate the threat. With the exception of the last case, the other patients were diagnosed

as being seriously ill with psychotic disorders, yet the diagnostic evaluations were not in essence different from those of the patients who had made unsuccessful suicidal attempts. One point worth noting is that the method for suicide was more determined in this group than in the other, and where one patient used barbiturates alone, the added measure was taken of using a hotel room to reduce the chances of early discovery. Five of the group were women, four were men, and the age range varied from 27 to 53 years, approximating the adult young to middle age group. A striking feature in these cases was the recurrence of a severe insoluble conflict with a key figure whose support was needed but not given. In a very real sense, it was a battle of life or death, and the suicidal act came only after many other avenues for resolving conflict had been tried without success. A thought-provoking fact is provided by the refusal of the relatives most deeply concerned to co-operate in taking protective measures. As a matter of fact, reactions of deep hostility to the patient were readily evoked, with the wish for the patient's death overtly expressed or clearly implied. In the therapy of these patients, transference ties were tenuous. The patients were too ill to work through ego distortions, as the psychic energy was mainly directed into a flight from overwhelming anxiety or into externalizing inner conflicts which created difficult reality problems. It was difficult indeed to avoid being manipulated by the incessant demands for support into a participation and strengthening of the patient's distortions.

#### DISCUSSION

Suicidal attempts, as distinct from suicidal gestures, occur in the course of serious mental illness and should be taken as an indication of a grave psychiatric disorder. The actual attempt usually comes at a time of acute exacerbation in a recurring highly important interpersonal conflict. The suicidal attempt represents and expresses a variety of internalized forces. Hostile destructive forces are self-directed in an overwhelming storm of rage and frustration. Additional motivation of great importance is the wish to die, in the attempt to gratify the hostile wishes, expressed or implied, of another person who is playing a crucial role in the patient's intrapsychic conflicts. Implicit in this manoeuvre is the hope for acceptance and forgiveness. Indeed,

when one compares the two clinical groups, whose patients seem approximately equally ill, the decisive factor making for the successful suicide appears to be the nonverbal command, consent or collusion that is reached between the patient and the person most involved in the psychic struggle, for suicide to become the final solution to the problem. Clinically the intensity of the wish to die appears to be the decisive factor, and the final outcome rests on a summation effect of environmental forces facilitating this wish. This is reminiscent of the Japanese suicide, which is culturally demanded as the best solution to redeem "loss of face".

These observations may be helpful in distinguishing the suicidal patient who can be carried as a "calculated risk" from the one whose acting out is inevitable. It also indicates the importance of early assessment of the patient's environment to evaluate the constructive and destructive forces with which the patient must cope. This material suggests that protective removal of the severely ill patient from a hostile and destructive environment can be a life-saving measure. However, it must also be understood that the struggle to the death between the sick patient and his often sick environment will precisely make it impossible for the therapist to alter the course of events for the patient in some cases. It then remains a personal matter for the therapist to decide whether or not he will withdraw from the case rather than continue as a helpless spectator.

The particular method for suicide is a matter of much interest in considering the whole problem of suicide, but observations on this matter are not to be included for discussion at this time. However, I would expect that study of this area would be well worth while.

#### SUMMARY

The suicidal attempt is the most common emergency for the psychiatrist in private practice. A review of recent literature on this subject emphasizes the high incidence of familial mental disorders in such patients, and the predominant view expressed is that the suicidal attempt is a symptom of a psychiatric disturbance which requires unhurried evaluation. The most common precipitating disturbance is an acute stressful situation which overwhelms the vulnerable ego and results in grossly distorted efforts at adaptation. The motivation of the suicidal attempt is described by Menninger and others as being determined by a complex of unconscious forces, the relative strength of which decides the outcome of the attempt.

Clinical observations on suicide are made on the basis of material drawn from the author's private practice. A total of 33 patients attempted suicide either while in psychotherapy or after the initial examination was carried out; 9 patients succeeded in their attempts. This material is described with reference to the suicidal technique, the diagnostic evaluations and the precipitating situation. Special attention is drawn to the fact

that a decisive factor in the successful suicide attempt appears to be the implied consent or unconscious collusion between the patient and the person most involved in the psychic struggle. The implications for management of the suicidal patient in office practice are discussed.

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#### RÉSUMÉ

La tentative de suicide représente en clientèle l'urgence psychiatrique par excellence. Un rappel des récents travaux sur ce sujet souligne la fréquence des antécédents mentaux chez ces malades. L'opinion la plus communément entretenu à l'heure présente est que le suicidant révèle une aberration psychiatrique dont l'évaluation ne doit pas être entreprise à la légère. Parmi les circonstances favorisantes la plus fréquente est celle par laquelle le sujet est poussé dans une position soudainement intenable qui vient à bout de sa vulnérabilité et écrase l'ego. Cette situation aboutit à des efforts d'adaptation grossièrement déformés. La motivation de la tentative de suicide serait déterminée d'après Menninger et d'autres par un complexe de composantes subconscientes dont les forces respectives décideraient du résultat de la tentative.

L'auteur a extrait ses observations cliniques des dossiers de sa propre clientèle. Il a vu jusqu'à présent 33 malades qui cherchèrent à se suicider au cours du traitement psychothérapeutique ou même dès la première entrevue. Neuf d'entre eux réussirent. Il évoque les techniques dont se servirent ces malades, les impressions diagnostiques qu'il posa et les situations qui précipitèrent ces tragédies. On souligne le fait que le facteur décisif des réussites de suicide semble être l'assentiment tacite ou la collusion subconsciente entre la victime et la personne la plus intimement impliquée dans cette lutte psychique. Les applications de ces remarques au traitement des suicidants en clientèle sont exposées dans le texte.

## Case Reports

### A CASE OF HYDRONEPHROSIS DUE TO FUNGUS BALL\*

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OF THE PATHOGENIC FUNGI which form ball-like aggregations the only ones commonly known are members of the *Aspergillus* species, usually *A. fumigatus* or *A. niger*.<sup>1-4</sup> We have not been able to find similar references to *Candida* species forming ball aggregates, hence this report. The name "fungus ball" to describe the condition is admittedly not very elegant, yet it conveys the situation, and unfortunately the term "mycetoma" is traditionally bound to the clinical condition of Madura foot.<sup>5</sup>

The patient was a 42-year-old woman of Central European origin who was first admitted to hospital in June 1957 with complaints referable to mitral stenosis. A mitral commissurotomy had been previously considered but rejected as inadvisable because of renal disease (presumed chronic pyelonephritis). On admission, she was short of breath, and on examination the heart was clinically enlarged and a diastolic rumble was heard at the apex; blood pressure was 178/110 mm. Hg. There was constant albuminuria up to 515 mg. %, and no specimen of urine received by the laboratory reached a specific gravity higher than 1.011 and none contained glucose. Her cardiac status improved with rest and digitalization, and she was discharged improved.

The second admission was on September 12, 1957, at the time of an influenza epidemic. She had a temperature of 104° F. which subsided fairly rapidly. Subsequently, she developed right-sided hemiplegia and died on October 8. During her hospital stay she received 43 injections of Dicysticin (a total of

12,900,000 penicillin G. procaine, 4,300,000 units penicillin G. potassium, 10.75 g. dehydrostreptomycin sulfate and 10.75 g. streptomycin sulfate).

Autopsy was performed five hours after death and the significant findings were as follows. The heart weighed 300 g., the left atrium was dilated and the mitral valve was thickened while the chordal tendineæ were shortened and thickened. The intact valve just admitted the tip of the small finger. No thrombi were found in the atrium, on the valve, or in the auricular appendix. The lungs showed bronchopneumonia and the spleen contained a fairly recent infarct. The left middle cerebral artery was obstructed by an organizing blood clot and the left internal capsule and adjacent nuclei evinced softening. The kidneys were not unusual in size or shape. The fibrous capsules were easily stripped to reveal a yellow-brown surface. On sections both cortex and medulla were blurred, and there was mottling of yellow. The renal pelvis and calyces on the left were normal, but on the right these were dilated and filled with numerous soft-putty-like, yellow unattached bodies about 2 cm. in diameter. These could easily be opened and a Gram stain of their contents showed numerous pseudohyphae.

Microscopically, all renal sections showed a similar picture. All glomeruli were abnormal, generally larger than usual, and the mesangium was thickened although not cellular. Generally they were remarkably bloodless. Bowman's capsule was not altered. In many of the glomeruli, segments of the capillaries were fused and non-patent, the whole being replaced by eosinophilic material (Fig. 1). These areas were occasionally adherent to the capsule. Elsewhere such areas were refractile and occasionally resembled the exudative type of Kimmelstiel-Wilson lesions.<sup>6</sup> The afferent artery and its pool<sup>7</sup> showed similar hyaline refractile change. The tubules occasionally contained protein casts; in some areas the proximal convoluted tubules were foamy and some were altered so as to resemble large macrophages (Fig. 2). Under polarized light "Maltese cross" refractile bodies were present in the lining cells. The renal "calculi" on examination had a variety of capsule of acellular protein material enclosing amorphous eosinophilic debris, numerous mycelia, ovoid yeast-like bodies and a few segmented leukocytes (Fig. 3).

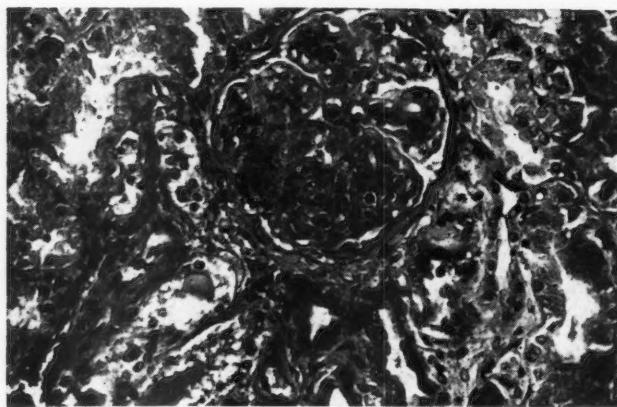


Fig. 1.—A typical glomerulus. Note the hyalinization of a segment. H. & E.  $\times 300$ .

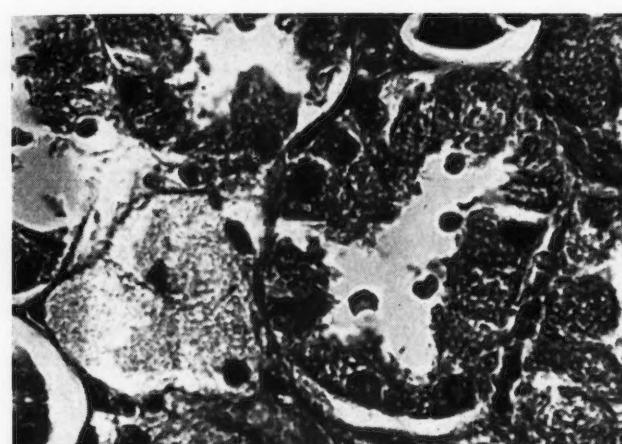


Fig. 2.—The small tubule appears lined by three large foamy cells. Examination under polarized light showed "Maltese cross" figures in many similar cells. H. & E.  $\times 630$ .

\*From the Departments of Pathology, Memorial and General Hospitals, Sudbury, Ontario.

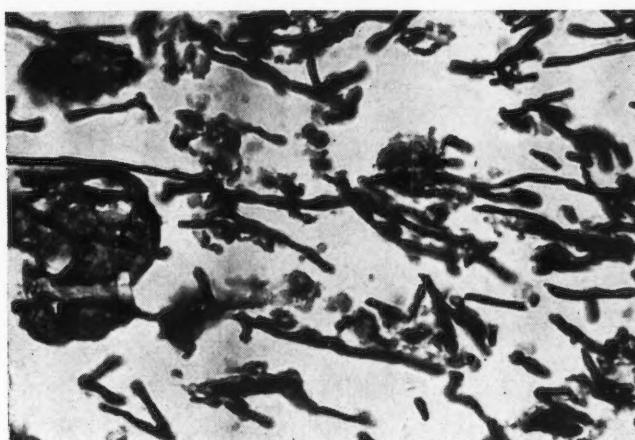


Fig. 3.—Section of a fungus ball. Numerous pseudohyphae are seen amid a small amount of proteinoid debris. P.A.S.  $\times 630$ .

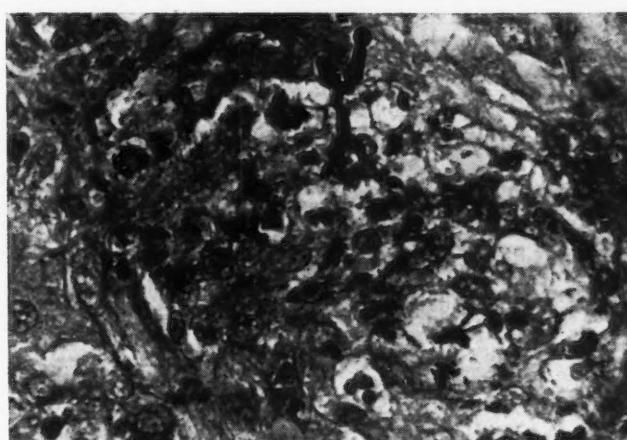


Fig. 4.—A miliary abscess in rabbit myocardium. At the periphery is a well-known yeast cell with pseudohyphae. P.A.S.  $\times 630$ .

### Mycology

The "calculi" were cultured on Sabouraud's dextrose agar and incubated at 22° C. After 48 hours, colonies developed which resembled *Candida*. The odour was not completely typical, however. One colony was subcultured to Difco chlamydospore agar and incubated at 22° C. for four days. No chlamydospores had developed after this time, although generally chlamydospores are abundant on this media in this period. After seven days atypical chlamydospores and small pseudohyphae appeared. The atypical chlamydospores were elongated and reniform in shape rather than the usual spheroid but they took up the trypan blue of the medium.

Subcultures were made in phenol red carbohydrate broth with the carbohydrate in a concentration of 3%. The yeast fermented glucose and maltose with production of acid and gas, but saccharose and lactose were not altered. Incubation at 37° C. and at 22° C. for 14 days failed to produce any additional fermentation. One ml. of a 1% suspension of the yeast, grown on Sabouraud's medium, in saline with penicillin (300,000 i.u.) added, was injected intravenously into a healthy adult rabbit. The suspension contained about  $1.7 \times 10^7$  *Candida* cells. After seven days the rabbit appeared moribund and was killed. At autopsy, there was miliary dissemination, especially in the myocardium (Fig. 4), lung and spleen. The kidneys were pale and swollen. Culture from the rabbit lesions yielded an organism identical morphologically, culturally and biochemically with the original culture.

The identity of the organism remains in some doubt, since it failed to produce chlamydospores after four days' incubation on Difco chlamydospore agar and produced atypical chlamydospores after seven days. It failed to ferment saccharose after prolonged incubation. The biochemical pattern is that of *C. stellatoidea*, but the cultural characteristics were unlike those of this organism. Further, the isolated organism proved pathogenic in a rabbit, a point said to be diagnostic of *C. albicans*.<sup>5</sup> It was concluded that the organism was an atypical form of *C. albicans*.

### DISCUSSION

Fungus ball obstruction of the kidney is surely an unusual occurrence, and we have been unable

to find reference to a similar case. The appearance of such a lesion in the kidney of a patient with chronic glomerulonephritis with lipid nephrosis raises the problem whether the unusual composition of the urine played a part in the pathogenesis of the condition. The diagnosis of focal endocarditic glomerulonephritis was rejected in the absence of bacterial endocarditis and in view of the long history. On occasion we have seen partially solidified proteinoid material in the renal pelvis of subjects with gross proteinuria (in the last case so observed, autopsy was performed five hours post mortem). If such material forms *in vivo* in patients with proteinuria, it is not improbable that it may form the nidus of infection. In a patient receiving high dosage of antibiotics, such an infection might well be with *Candida*. In this case, no other focus of infection was found, but it is believed that the above outlines the sequence of events. It is possible that the organism entered through the urinary tract or was excreted from the blood stream through the severely damaged glomeruli, a primary site elsewhere having been overlooked.

### SUMMARY

A case of fungus ball of the renal pelvis causing hydronephrosis is described in a patient with chronic glomerulonephritis and lipid nephrosis.

The organism is described and was identified as an atypical form of *Candida albicans*.

The etiological factors are discussed.

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## ADRENAL CORTICAL CARCINOMA ASSOCIATED WITH HYPOGLYCAEMIA\*

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IN RECENT YEARS there have been several reports of patients with large tumours in the upper abdomen or lower chest, in whom the main symptom and sometimes the cause of death was a marked hypoglycaemia.<sup>1-11, 13-15</sup> The direct causal relationship of the neoplasm to the low blood sugar level was indicated in some instances by the disappearance of the hypoglycaemia after resection of the tumour<sup>3, 6, 9, 10, 15</sup> and its recurrence with regrowth.<sup>6</sup> Skillern *et al.*<sup>14</sup> believed that such lesions were of ectopic islet cell origin. Yet insulin assays, although only rarely carried out on these tumours, were negative in at least two previous instances.<sup>10, 11</sup> In the case to be described here, not only was insulin absent from the main tumour and its metastases but the pancreas also had only a normal insulin content, so that the fortuitous presence of a small functioning islet cell adenoma could be excluded.

**Clinical summary.**—A 26-year-old woman developed attacks of low back pain, followed within a few months by enlargement of the abdomen and episodes of epigastric discomfort. One and a half years later she consulted a doctor for increasing weakness. A low blood sugar level was found and a high carbohydrate diet prescribed. After a further six months she went to bed with an attack of especially severe back pain and marked distension of the abdomen. Within two days she became irrational, then lapsed into coma and was admitted to hospital.

The patient was pale and had a cool moist skin, pulse rate 110, blood pressure 130/70 mm. Hg, respirations 18. The reflexes were hyperactive and there was prolonged ankle clonus, but the plantar responses were absent. The extremities were rigid and extended with a bilateral carpopedal spasm. A large mass was palpable in the left upper quadrant of the abdomen, extending to 4 cm. below the left costal margin.

The blood sugar was 37 mg. %. Urine, haemoglobin level, white blood cell count, sedimentation rate, serum amylase, non-protein nitrogen (N.P.N.), serum electrolytes, serum calcium, liver function and the spinal fluid were all normal. An electrocardiogram showed sinus tachycardia at 110 per minute; an electroencephalogram was diffusely abnormal from a deep midline origin (blood sugar level at that time was 96 mg. %). Radiographs of the chest, skull and lumbo-sacral vertebrae were normal. A barium meal revealed an extrinsic retroperitoneal mass. An intravenous pyelogram was normal, but the left kidney was depressed and rotated.

After intravenous glucose administration the patient became conscious, but the blood sugar could be maintained at normal levels only by constant oral or intravenous glucose therapy.

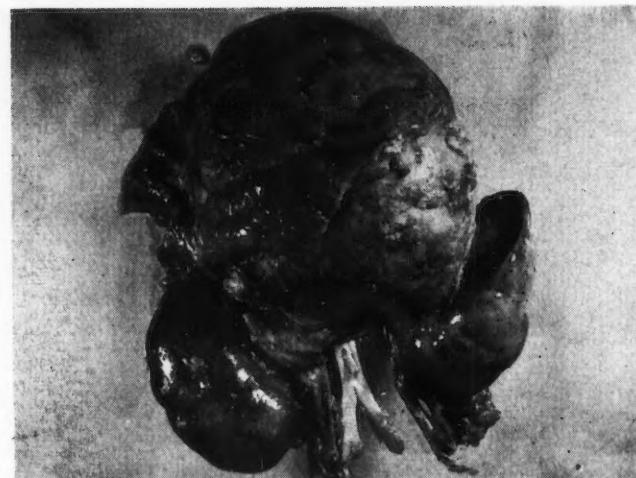


Fig. 1.—The left adrenal gland is replaced by a large globular tumour which has indented the left kidney. The pancreas lies in front of the tumour.

A laparotomy was undertaken to determine the nature of the abdominal mass. A large tumour was found at the upper pole of the left kidney, and metastases were noted in the liver. The pancreas lay in front of the tumour but appeared normal. Biopsies from the main mass and a liver metastasis showed an anaplastic carcinoma. In Gömöri stains some of the cells were thought to contain a few indefinite blue granules, and partly on this basis, but more so because of the clinical history, a functioning islet cell carcinoma was diagnosed.

During the next weeks the maintenance of adequate blood sugar levels proved increasingly difficult. Hypoglycaemic episodes became frequent, and between attacks the blood sugar remained fixed at 30-50 mg. %. The patient died about one month after hospitalization during an attack in which no blood sugar was demonstrable.

### POSTMORTEM EXAMINATION

**Gross findings.**—The body was that of a somewhat obese young woman. The abdomen was protuberant and contained marked lower abdominal striae and a recent laparotomy scar. Slightly excessive hair was present on the upper lip and chin, but otherwise the female sex characteristics were quite normal.

The main lesion was found in the upper abdomen and consisted of a very large globular tumour mass, measuring 18 cm. in diameter and weighing 2200 g., which had replaced the left adrenal gland (Fig. 1). The tumour on section was somewhat lobulated, fleshy, soft and white, with a large yellow necrotic centre. It had depressed and indented the left kidney and had displaced the aorta and inferior vena cava to the right of the vertebral column. The body and tail of the pancreas were flattened and lay across the front of the tumour but despite some adhesions could be freed by blunt dissection. Worms of putty-like material could be squeezed from the tail of the pancreas in the area of the previous biopsy. Although the tumour was mostly encapsulated, it had penetrated the capsule at the superior pole, invaded the left leaf of the diaphragm and had seeded metastatic nodules on its pleural surface. The left pleural cavity contained 500 c.c. of clear straw-coloured fluid.

The tumour filled the left renal vein and extended from there into the inferior vena cava, which was

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completely blocked, up to about 1 cm. from the liver. The tributaries of the caval vein below the block were engorged, and especially the pelvic veins were markedly tortuous and partly thrombosed. Both lungs and the liver were studded with metastatic nodules measuring 1 to 6 cm. in diameter. The lymph nodes were uninvolved. The lungs were oedematous and contained small emboli and infarcts.

The other organs, including the right adrenal gland, were grossly normal, although all tended to be excessive in weight.

*Microscopical findings.*—The tumour in the primary area and metastatic deposits showed identical histological features. It consisted of sheets of fairly large polygonal cells with eosinophilic or vacuolated cytoplasm and round or oval nuclei (Fig. 2). Occasional giant cells with very large hyperchromatic nuclei were present and mitotic figures were abundant. Fat could be demonstrated in the vacuolated neoplastic cells in frozen sections stained by Sudan III. Gömöri stains of the tumour material were uniformly negative, while satisfactory staining of the beta cells in the islets was obtained by similarly treating sections of the pancreas. Areas of necrosis were scattered through the tumour. The blood supply was abundant and consisted of many thinwalled and sinusoidal vessels.

Several blocks taken from the pancreas showed only normal acinar and islet tissue. In the region of the previous biopsy, fat necrosis, foreign body giant cells and granulation tissue were present.

In the liver and spleen there were small foci of extramedullary haemopoiesis, and a few megakaryocytes were lodged in the sinusoids. Bone marrow from a lumbar vertebra was normal. Although one cannot exclude the possibility that the extramedullary haemopoiesis was associated with metastases to bone, there was no radiological evidence for this assumption. Since adrenal cortical hormones stimulate the bone marrow to overproduction of cells,<sup>17</sup> hormonal activity of the tumour may have been responsible for the blood formation in liver and spleen.

Sections of the liver stained for glycogen were negative.

The lungs contained small organizing infarcts.

In the brain, some of the larger nerve cells in the cerebral cortex were shrunken, eosinophilic and devoid of Nissl substance, a change compatible with anoxia or hypoglycaemia.

The other organs, including the pituitary gland and right adrenal, were histologically normal. The breasts

and female genitalia showed the physiological activity appropriate for a young woman.

*Pathological diagnoses.*—Carcinoma of the left adrenal cortex; tumour invasion of diaphragm, left renal vein and inferior vena cava; metastases to liver and lungs; left hydrothorax; pulmonary oedema; hypoglycaemic nerve cell changes in brain; pulmonary emboli and infarcts; extramedullary haemopoiesis of liver and spleen; fat necrosis and foreign body granuloma of tail of pancreas; macrosplanchnia.

*Insulin assay* (Dr. G. A. Wrenshall).—Portions of the main tumour mass, metastases to the lung and liver, the right adrenal gland and the entire pancreas except for the blocks examined microscopically were assayed for insulin. All specimens of tumour and the right adrenal gland were negative for insulin, while the pancreas contained approximately 1 unit per gram, a low normal value.

#### COMMENT

To date no satisfactory explanation exists for the hypoglycaemia associated with non-pancreatic tumours. The contention of Skillern *et al.*<sup>14</sup> that these lesions are of ectopic pancreatic origin is hardly tenable in view of the histological diversity among the neoplasms reported. Five,<sup>1, 4, 7, 15</sup> including our own, were interpreted as carcinomas of the adrenal cortex and in three the diagnosis was supported by a raised urinary output of 17-ketosteroids. A sixth case was of a large adrenal cortical adenoma.<sup>9</sup> There were further two fibromas,<sup>11, 13</sup> four fibrosarcomas,<sup>3, 5, 10</sup> one retroperitoneal sarcoma,<sup>2</sup> one liposarcoma<sup>6</sup> and two cases of pseudomyxoma peritonei.<sup>8</sup>

The suggestion that such tumours elaborate an insulin-like substance<sup>1</sup> has recently received support by August and Hiatt,<sup>3</sup> who were able by means of the Vallance-Owen test to demonstrate in their case of a pleural fibrosarcoma the presence of an agent which promoted the uptake of glucose by the isolated rat diaphragm. On the other hand, insulin assays on other tumours,<sup>10, 11</sup> including our own, were negative. Hines<sup>6</sup> has suggested that some metabolic product of the tumour stimulates the pancreas to a greater output of insulin. Alternatively he has suggested that a release from the tumour of some substance requiring excessive carbohydrate for its metabolism might have occurred, or that a similar demand by the rapidly proliferating neoplastic cells might exist. Our data shed no new light on these possibilities.

It is tempting to postulate a hormonal disturbance of the control of the blood sugar level in patients with an adrenal neoplasm.<sup>4</sup> Although increased activity of the adrenal cortex usually leads to hyperglycaemia, children with an overgrowth of the androgenic zone may exhibit the Addisonian syndrome with a low blood sugar level.<sup>16</sup> Selye<sup>12</sup> found that rats given desoxycorticosterone acetate and then exposed to stress developed a marked hypoglycaemia, thus proving that excess of one adrenocortical hormone can suppress the action of another one.

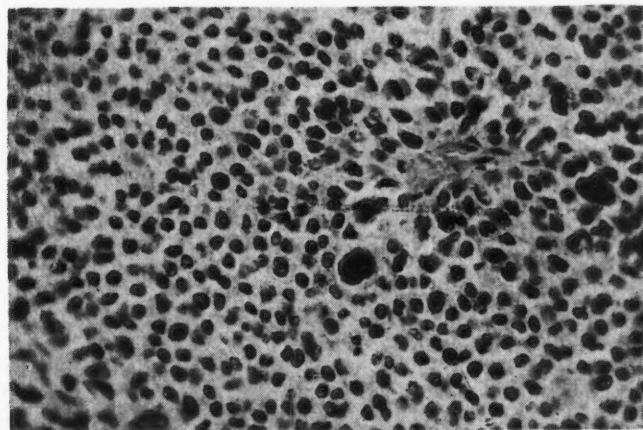


Fig. 2.—Typical microscopical field of tumour. Haematoxylin and eosin,  $\times 375$ .

Finally, Lawrence<sup>7</sup> and Seckel<sup>11</sup> suggested that these tumours, by virtue of their location and large size, stretch the sympathetic nerve trunks or receptors in the liver, adrenals and pancreas and thus interfere with glycogen mobilization. This theory is perhaps the most plausible one since it takes into account the features common to all the tumours and is thus applicable to the whole group.

#### SUMMARY

A case is reported of a large adrenal cortical carcinoma in a young woman, associated with severe hypoglycaemia which led to the death of the patient. The literature on similar cases and current theories on the pathogenesis of the hypoglycaemia are briefly discussed.

We are indebted to Dr. G. A. Wrenshall, Banting and Best Department of Medical Research, University of Toronto, for the insulin determinations.

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## Special Article

### MAN, MACHINES AND EMOTIONS\*

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EVER SINCE MAN gave up the security of the tree tops, and the advantages of prehensile toes and a tail, he would appear to have been plagued with feelings of insecurity. Man, by his actions, gives the impression that he has never really adjusted to the uncertainty of life at ground level. From prehistoric times his unique ability to think has been concentrated on devising ways and means of overcoming his physical shortcomings, and removing threats, real or imagined, that make life on terra firma a somewhat hazardous business.

Being but human, Man has shown a consistent propensity for misapplying his ever increasing

\*Based on an address given at a two-day seminar on mental health in industry, sponsored by the Canadian Mental Health Association, Calgary, March 1958.

technical skills. He now possesses the skill to obliterate not only himself, but also all he has ever achieved. This is naturally a matter for some concern. Though man has progressed from the sharpened flint to "the ultimate deterrent", it must also be remembered that the abacus has been replaced by UNIVAC, the ox-drawn cart by the jet transport, the witch's brew by modern medications, and even psychiatry can be regarded as an advance on the oracle or the more bloodthirsty of exorcistic rituals. The maintenance of a state of balance and proportion is essential, lest contemplation of man's more spectacular technical skills produce a state of petrified pessimism. To counterbalance this gloom and despondency, it seems advisable to look at some new production techniques—techniques that may remove much of the drudgery from human life, and allow man the time and opportunity to devote himself to worthwhile and constructive pursuits.

#### MECHANIZATION v. AUTOMATION

In the past 50 years or so significant changes have occurred in the approach to the problem of mechanical aids and production techniques. No longer is the problem merely that of devising more efficient means of placing more horsepower at the disposal of the individual worker. The problem now is to find methods whereby more and more goods can be produced by fewer and fewer men. Until now the "assembly line" has been regarded as the ultimate in the mass production of goods. The idea of bringing constituent parts to workers instead of workers taking the parts to an assembly site was regarded as revolutionary as well as impractical. It required a Henry Ford to prove that the idea was not only practical but also of considerable economic worth.

Assembly-line production was undoubtedly a great advance. Goods of great complexity could be produced in great numbers at reasonable prices. Productivity per worker reached undreamt of heights. But the method contained one glaring imperfection. Its success depended on its human component—a component that has always been famous for its inability to comply with rigid specifications plus its susceptibility to breakdown. The exclusion of such an unreliable bit of equipment from any production system would obviously be a great technological achievement.

#### AUTOMATION

How could this dream be realized? As usual, it took a war to provide the motivation, funds, and brainpower. Guns had to be made to fire with accuracy at distant fast-moving targets. Human brain and brawn were too slow for such a job. The computer-aimed-and-fired weapon came into being. At long last inanimate machinery evidenced some purposeful action without human interference. If such techniques could be applied to engines of war, they obviously could be applied to the less stringent demands of peace.

This technique of machines supervising other machines and continuously producing finished goods without humans playing the time-honoured role of "workers" is the essence of automation.

"Automation is the technology of automatic working in which handling methods, the processes and the design of the processed material are integrated to utilize as is economically justifiable *the mechanization of thought and effort* in order to achieve an automatic and in some cases self-regulating chain of processes."<sup>1</sup>

#### AUTOMATIC CONTROL—"FEED-BACK"

Automatic control is now possible as a result of advances in electronics and the incorporation and utilization of feed-back into circuitry design. In a fully automated factory the worker has been replaced by a control unit which receives instructions from the master computer. The control unit, in its turn, receives information from a sensing unit—the electronic usurper of the human inspector; the quantitative differences between these two units initiate change into the system to eradicate "error". This self-regulating mechanism and error-removing action is "negative feed-back". The degree of allowable error is stored in the control unit's "memory". Such a system will maintain the various processes within predetermined tolerances for the entire production run.

The master computer is "programmed" or "taped" with the data necessary for the particular processes involved in the making of the product. This programming is worked out in advance by suitably trained persons. The program is then "fed into" the master computer and the entire process of manufacture then carried out without any direct human intervention—i.e. from the raw material to the finished, packaged product. All intermediate processes and procedures are taken care of by batteries of minor sensors and controls following to the letter the program fed to the master computer control unit.

It would appear then that Utopia is close! At long last man has gained sight of his goal—a limitless supply of goods spewed out by machines of his own making and obedient to his command—goods that will enable man to lead the "full life" he has always dreamt of. Why then the despondency, anxiety and gloom that pervades workers, unions and managements? For an answer, it is necessary to take another look at this distant relative of ours who descended from the tree tops in prehistoric times.

#### PRIMITIVE v. MODERN MAN

Anthropometric studies of our "primitive" ancestor indicate that the size and cubic capacity of his brain was similar to our own. The markings on the inner side of the skull do not indicate any less complexity of brain foldings. It is presumptuous of us to assume that the inherent capacity to learn was significantly less in our remote ancestor than in ourselves. Admittedly there was less knowledge to assimilate, but whether our predecessor's inborn intelligence was less is a moot point. Ever since man has made permanent records of his thought processes he has supplied adequate evidence that original thought is not one of the prerogatives of modern man.

It follows therefore that all of us are anthropological Jekylls and Hydes—our emotional

"maturity" differs but little from that of our "primitive" ancestors. This is not really so startling, or unlikely, if we make the time scale during which life has existed on this earth one hundred years. Then human life has existed for one month and civilization in the broad sense for a mere three hours. These three hours have seen tremendous achievements, but this brief existence has not been of sufficient duration to allow us to shed our primitive emotional ancestry. It is this disparity between the rates of man's technical and emotional development that is the crux of today's anxieties. An historical perspective such as this helps us to understand the apparent inconsistencies that characterize human behaviour whether at the individual or international level.

#### THE AUTOMATIC FACTORY

To the casual visitor a fully automated plant appears to provide the perfect work environment. Its location is usually rural or suburban. "A home away from home" was obviously at the back of the planner's mind when he conceived the idea of the plant. The industrial architect has made the idea a reality. No longer is it necessary for plants to be located close to centres of population, for manpower demands are minimal and any skills required will be taught on the plant site. The essential needs of such a plant are only two in number—adequate supply of power and suitable means of transportation so that the raw material may be easily brought and the finished product easily despatched. As automation increases in scope there will undoubtedly be a marked "de-urbanization" of industry.

Work areas in such a plant are reminiscent of the glamorized laboratories so frequently seen on the movie screen. The worker's white coverall puts a surgeon's to shame. The lighting is shadowless, glareless and of optimum intensity for working ease. The colours of walls, ceilings and equipment are the result of lengthy consultations between interior decorator and industrial psychologist. Gone are the toxic hazards, the rupture-producing strains of heavy manual work. Even the temperature, humidity and air movement meet the rigid standards of the expert in "human engineering".

Surely in such an environment the human attendant will be happy with his machine. Yet on second glance there is something about a plant of this type reminiscent of the advertisements showing contented cows producing a well-known brand of milk. Undoubtedly such a plant is a marvel of functional planning and layout, but is it the ideal *human* work environment?

From all accounts it would appear that human workers cannot be equated with Mr. Borden's contented cows. Demands for "lonely money" are being heard from the workers in fully automated refineries. "Tension" and "think money" will doubtless be part of the wage earner's take-home pay in the future. Even the initial response of the worker when first introduced into such an industrial paradise is not what management might expect. "I'd rather have to work hard for eight hours than do nothing physical but have to be tense for eight hours, the way I do now." "On my

old job . . . my muscles got tired. I went home and rested a bit and my muscles were no longer tired. On this new automatic mill, your muscles don't get tired, but you keep on thinking, even when you go home."<sup>2</sup> However, most humans can adapt themselves to most situations. Eventually the feelings of fatigue, tenseness, and resentment lessen in the more adaptable. The more rigid usually quit. Gradually in the workers who remain an increasing sense of job satisfaction is felt. These satisfactions now arise from precisely those characteristics of the automated factory that originally caused the fatigue, strain and resentment—the necessity to watch all the time, to act on split-second notice, to think more and to endure tension. On a previous occasion, mention has been made of six factors contributing to job satisfaction: status and prestige; sense of belonging; approval; creativity; money and security.<sup>3</sup> The worker who has successfully coped with the emotional conflicts of the settling-in phase, and has made the physical adjustments necessary to enjoy work in the fully automated factory, has in these adjustment processes acquired status, prestige and a sense of belonging. He is now one of the *elite* of the labour force—the highly trained, skilled technician.

#### CREATIVENESS

Creativeness deserves special mention. It might be thought that creativeness plays but little part in the satisfaction gained from employment in an automated plant. Quite the reverse is the case. In the assembly-line technique a worker spends his eight hours performing repetitive tasks. In an automated plant he becomes part of a small select crew closely involved with the product from its initial process to its final packaging. The product grows before his eyes. He has been involved with its inception and he gains satisfaction from seeing the completed product leave the plant. He gains additional satisfaction from the knowledge that his "watching" and constant readiness to deal with recalcitrant machines has enabled the process of manufacture to continue without money-consuming stoppage. Responsibility for the smooth running of a million-dollar automatic system has been shared by himself, a few fellow technicians and maintenance men.

Success in a creative enterprise provides one of the greatest possible satisfactions in life. This personal satisfaction is added to further in the case of the worker in the automatic factory. It is a satisfaction shared with others. In consequence, not only are several of the worker's basic instincts satisfied, but the entire work group experiences the same emotional gratifications. Group cohesiveness is thereby enhanced. Automatic production no longer relies on independent, unrelated groups but rather on interplay between inter-related groups of men and their machines. Hence success in the operation of an automatic factory necessitates the participation of all—machines, technicians, maintenance crews, engineers and management. Many of the basic emotional needs so glaringly absent in the impersonal, monotonous assembly-line are present in the close-knit community of the automatic plant.

#### MONEY

Perhaps money and its significance should be commented upon further. The continuous-production technique of the automatic factory upsets the long established practice of "piece work" as the incentive to greater productivity. The output of goods is no longer dependent on individual effort, or even on the efforts of groups, but rather is the expression of the smooth integration of all plant personnel and the machines—from maintenance men to top administration.

This fact has caused management to change its traditional attitude to the worker and his work. If, as now would appear to be the case, the success of an automated factory depends on a "one for all, all for one" type of approach, then obviously measurement of work can only be correlated with the output of goods and total output becomes the criterion of wages. If "piece work" is becoming an antiquated concept in the automatic factory, so also is the time-honoured distinction between "staff" and "pay roll". Where does one end and the other begin? It is highly probable that the introduction of automation techniques in industry and business will speed up the trend to yearly salaries and profit-sharing plans for all employees.

The worker in the automatic factory would thus appear to have solved many of the emotional problems that so frequently arise out of the work environment. But some still remain and will doubtless grow in importance as more of the labour force becomes involved with automatic equipment.

#### PROMOTION

If "piece work" has been the traditional method by which a worker may increase his pay, gradual ascent, rung by rung, of the promotion ladder has been the accepted method of increasing status. The automatic factory makes a break with this tradition. The self-regulating machines have removed many of the rungs. Seniority is not the ideal criterion by which to judge a man's ability to cope with new and increasingly intricate machinery. Experience is not a substitute for technical "know-how". Perhaps "ruts" rather than "rungs" might be a better term to describe a worker's position in the hierarchy of the automatic factory. How can this state of affairs be remedied? The answer, of course, is through higher education.

#### EDUCATION

This fact has not gone unnoticed by the worker. The connection between promotion and education soon makes itself apparent in the small labour force of the automatic factory. This is reflected in the tremendously increased enrolment by such workers in an ever-widening variety of subjects offered by university evening courses.

But technical "know-how" is not enough. The understanding of human relations assumes more and more importance as management has to depend more and more on fewer and fewer key personnel. Technical "know-how" will be valueless

if those possessing it are ignorant of humans and machine-men relations. The graduate engineer will have to apprentice himself to the experienced foreman to learn about people. The experienced foreman will be forced to acquire new knowledge of a technical type from the graduate engineer. With the ever increasing integration of men with machines, it is now impossible for foremen and engineers to function efficiently in splendid isolation.

Education will have to change in scope and purpose in this era of scientific and technological advancement. High schools will have to drop the pleasure principle and concentrate on the acquisition of knowledge for its own sake. University education must be made broader and more comprehensive. Graduates must be mature competent individuals, not animated slide rules that regard people as annoying encumbrances to progress. With greater knowledge supplied the high school graduates, and a broadening of interests manifest in the products from the universities, it should then be possible to view future technological developments with eager anticipation. If these changes in our educational system do not occur, technological and scientific advances elsewhere will be viewed with fear and anxiety.

#### LEISURE

The present system of inadequate and misguided education has produced the next problem — the worthwhile utilization of leisure. Leisure time, i.e. time not spent at place of work, is going to increase. "To be able to fill leisure intelligently is the last product of civilization and at present very few people have reached this level."<sup>4</sup>

Modern technique has made it possible to reduce drastically the amount of labour necessary to maintain a satisfactory standard of living. This was evident during man's last unregulated emotional outburst. In spite of millions of the labour force in uniform, health, and nutrition did not suffer, nor were any essential material goods in significantly short supply. We should be glad that it is no longer necessary for a worker to labour long hours to provide himself and others with the basic comforts of life. Instead of eyeing with democratic contempt the leisured classes of old, we should be proud to belong to the leisured masses of today.

Intelligent utilization of leisure puts the onus on the individual. It demands making a choice or reaching a decision. Making a choice or reaching a decision necessitates some thought—an unpleasant and unusual chore in this day and age when "they" make the decisions for us. How much simpler to "work" the regulation eight-hour day and in a state of so-called mental exhaustion enjoy our leisures in a non-participant passive manner. We can all become "Walter Mittys" with the aid of visual entertainment media and so satisfy our repressed urges and aspirations. Or we can pay to watch, and exhort vociferously some paid gladiators in an arena, enabling our own feelings of hostility and resentment to be released in the process.

Is this gross abuse of leisure capable of rational explanation? Perhaps, if it is remembered that most people nowadays spend most of their working time at a task providing no outlet for latent or potential creative ability. Constructive use of leisure time would undoubtedly redress the balance. But the conformity of thought and action brought about by the monotony of an eight-hour shift five days a week stifles any such tendencies. Over the years the worker will become as stereotyped and unthinking in his leisure hours as he is whilst on the job. The mental inaction during his hours of leisure is but an extension of his state of mind during his hours of work. To break such a pattern is difficult.

The worker in an automatic factory comes from an entirely different work environment. Admittedly his physical activity is minimal, but mentally he is never at rest. Responsibility is entrusted to him in the shape of machines and materials. His knowledge of the processes involved is comprehensive. His thinking is integrative. His decisions have to be made with speed. This worker is not the Charlie Chaplin of "Modern Times"— an insignificant cog in a huge machine, but a responsible individual able to think, reason and act. Surely it is not being unduly optimistic to assume that such a worker will find his leisure more satisfying than did his counterpart on the assembly line.

#### CONCLUSION

Automation may be just another step in our technological progress but the concepts behind a self-regulating automatic process have far-reaching implications for mankind.

Man by the practical application of negative-feed-back has created beautiful systems of self-regulating machines. Unfortunately there is no evidence to suggest that man's emotions have the benefit of an analogous self-regulating mechanism. If anything, man has the attributes associated with a system plagued with positive feed-back. Such a system has the doubtful distinction of exhibiting an ever increasing state of instability that if left uncontrolled ends up in a state of chaos.

Man's own past history makes intelligible reading if today's principles of feed-back are utilized in interpretation. Viewed in this light, man's checkered past is not a sordid tale of bigger and better wars brightened by a few short-lived renaissances. Instead history takes the form of cycles of human action and interaction, each cycle manifesting the unfortunate consequences of positive feed-back. At the individual level this is of no consequence, but at national and international levels today the culmination of the present cycle in the usual man-made form of chaos can spell doom for our civilization. Man would be well advised to stand back and view these machines of his in a humble and contemplative manner. By some quirk of fate these man-made machines have attributes that man himself so sadly lacks, yet so desperately needs if he is to survive.

If modern man is to enjoy the benefits of his scientific technical advances he will have to apply the self-regulatory mechanisms of his machines to

his own unconscious primitive urges. If this self-regulation can be achieved, our present gloom and despondency will disappear. Perhaps it is possible to detect such self-regulatory mechanisms at play in the world today.

It would appear that national prides can be soothed by blasting scientific bric-à-brac into outer space. Aggressive tendencies are now relieved by periodically polluting the atmosphere with radioactive wastes. International hostilities are apparently capable of harmless release by name calling at international gatherings. These innocent amusements represent a considerable advance in human self-regulatory mechanisms. It is to be hoped such pastimes will long remain satisfying. Unfortunately history indicates that play periods in the field of international affairs tend to be short-lived. If this present play period should follow the pattern of those in the past, future historians will be able to demonstrate yet another cycle of steadily increasing human instability ending in

chaos — so reminiscent of a positive feed-back system. Man would not tolerate such a system in his automatic machines, but he appears powerless to eradicate the defect in himself.

"Ever since history began, the majority of mankind has lived under a load of poverty and suffering and cruelty and have felt themselves impotent under the sway of hostile and impersonal powers. These evils are no longer necessary to the existence of civilization; they can be removed by the help of modern science and modern technique provided these are used in a humane spirit and with understanding of life and happiness".<sup>5</sup>

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## SHORT COMMUNICATION

### DIPIPANONE HYDROCHLORIDE (PIPADONE) AS A PRE-DELIVERY SEDATIVE AND ANALGESIC

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A PRE-DELIVERY SEDATIVE, to be of maximum value, must relieve discomfort for the patient quickly, efficiently and for a reasonable period of time. It should not delay or prolong labour and should have little or no adverse effect on fetal respiration.

For some years meperidine hydrochloride (Demerol) and alphaprodine hydrochloride (Nisentil) alone or with scopolamine have been the drugs of choice in this centre.

The object of this report is to assess the value of dipipanone hydrochloride as a pre-delivery sedative. The drug has been given in strengths of 20 and 25 mg., alone or in combination with barbiturates or scopolamine. One hundred public ward cases at the Winnipeg General Hospital have been studied. The results obtained with meperidine on 50 occasions, either alone or with scopolamine, have been recorded for comparison.

The injections were administered by the nurses on the labour floor, who were also responsible for

recording their impressions of the patient's response. An effort was made to give the pre-delivery sedative at approximately the same stage of labour, multiparæ as a rule being given sedatives at an earlier stage of cervical dilatation than the primiparæ. The relief of pain and sedative effect were recorded by the nurse as satisfactory or unsatisfactory. Side effects such as dizziness, nausea and vomiting were also noted. Apgar's<sup>1</sup> method of assessing neonatal condition at one minute of life is followed in the Maternity Division of the Winnipeg General Hospital, and the Apgar rating was applied in these cases in an attempt to assess the degree of depression of the infant's respiration. Results of using dipipanone and meperidine are compared in Table I. The patients are divided into primiparæ and multiparæ.

Where meperidine or meperidine with scopolamine was used, 94% had a satisfactory response, compared to 56% of those given dipipanone alone or in combination with a barbiturate or scopolamine. This lack of response was most noticeable in the primiparous group, where only 34.5% had adequate relief of pain after the administration of dipipanone. Side effects were not severe in any patient, although nausea and occasional vomiting were encountered in 11% of those receiving dipipanone.

TABLE I.

	<i>Drug used</i>	<i>Number of cases</i>	<i>Number of injections</i>	<i>Side effects</i>	<i>Relief of distress</i>		<i>% Satisfactory results</i>
					<i>Unsatisfactory</i>	<i>Satisfactory</i>	
Primigravidæ	Pipadone.....	26	26	5	17	9	34.5
	Demerol.....	21	26	0	1	25	96.1
Multiparæ	Pipadone.....	74	74	6	27	47	63.5
	Demerol.....	21	24	0	2	22	91.6
Totals	Pipadone.....	100	100	11	44	56	56.0
	Demerol.....	42	50	0	3	47	94.0

TABLE II.—APGAR RATING

	Drug	9-10 No depression	7-8 Mild depression	6 or less moderate to severe	% moderately depressed
Primigravidæ	Pipadone.....	20	3	0	0.0
	Demerol.....	10	7	4	19.0
Multiparæ	Pipadone.....	46	7	10	15.8
	Demerol.....	17	4	0	0.0
Totals	Pipadone.....	66	10	10	11.6
	Demerol.....	27	11	4	9.5

TABLE III.—RESULTS OF ADMINISTRATION OF DIPIPANONE TO GYNAECOLOGICAL PATIENTS

Diagnosis	No. of patients	Dosage	No. of injections	Relief obtained	% of	
				Satisfactory	Unsatisfactory	satisfactory results
Postoperative.....	5	20 mg.	26	22	4	84.6
	6	25 mg.	14	14	0	100.0
Carcinoma of cervix, Stage 4.....	1	30 mg.	3	3	0	33.3
	3	20 mg.	4	1	3	
Pelvic inflammatory disease.....	1	40 mg.	2	1	1	0.0
	17*	25 mg.	1	0	1	
Totals.....	17*		50	41	9	82.0

\*Two of the patients had varied doses.

Table II indicates the Apgar ratings recorded, and notes the percentages of infants with moderate depression of respiration. The numbers are too few to be statistically significant but are approximately the same in both series. Factors, other than sedation, which may lead to depression of the infant have not been assessed.

It is of interest that infants with moderate depression in the meperidine-treated group were all first babies, while those with depression in the dipipanone series were all born to multiparæ. Since the time interval between sedation and delivery averaged one and a half to two hours longer in the primiparæ, this would suggest that the maximum depressive action of meperidine occurs later than that of dipipanone. Only one infant had very serious depression, having an Apgar rating of 2. The other ratings varied from absence of depression to a depression of moderate degree. None of the infants died. The number of infants with depression is high but, as previously stated, the figures have not been corrected for other contributing factors.

A smaller series of 15 patients on the public gynaecological ward were given dipipanone for the relief of pain due to the conditions outlined in Table III. A total of 50 injections were administered. The figures show a satisfactory response to the drug after 82% of injections. Seven of the doses causing little or no relief were 20 mg., and three of the seven were used for one patient with advanced carcinoma of the cervix. This patient was an extremely apprehensive new Canadian who did not speak English. Forty mg. of dipipanone was given to this same patient on two occasions, one injection giving only slight relief and the other satisfactory relief of pain. The patient with pelvic inflammatory disease had no relief of pain after 25 mg. of dipipanone. Satisfactory relief of post-operative pain was obtained in 100% of patients who received 25 or 30 mg. of the drug.

Side effects were minimal; dizziness was complained of twice and nausea once.

#### CONCLUSIONS

It is felt, as a result of this study, that dipipanone hydrochloride is not as effective as meperidine

hydrochloride in the relief of distress in the first stage of labour. This is especially true in the primiparous patient. Our findings are not in agreement with those of other investigators.<sup>2, 3</sup>

It is our impression that the lack of hypnotic effect exhibited by dipipanone accounts for the poor results in the tense and often apprehensive patients, particularly those in labour for the first time. The use of grain 1/150 scopolamine with dipipanone increased its efficiency as a sedative but appeared also to increase the hazard of respiratory depression in the infant. No significant difference was noted in the number of infants with depression in the two series.

We are in agreement with previous investigators<sup>2, 4</sup> that dipipanone is an effective analgesic and that it has little hypnotic action.

It is our opinion that dipipanone is of most value as a postoperative analgesic. In the postoperative period the cooperation of the patient through early active movement and deep breathing exercises is advantageous, and the lack of hypnotic effect facilitates this cooperation. Twenty-five mg. appears to be the optimum dose for the patient of average size.

The variable pain threshold of patients and the different opinions of the nurses regarding degree of discomfort and relief, progress of labour and amount of cervical dilatation all tend to make the foregoing method of assessment inadequate, but evidence for the above impressions seems to be indicated in the figures obtained.

I wish to thank Mrs. A. Morton and her staff for their help in carrying out this survey, and Dr. Brian D. Best and Dr. C. J. McFarlane for their assistance in preparing the paper. The dipipanone hydrochloride used was kindly supplied by Burroughs Wellcome & Co. (Canada) Ltd.

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## THE SOCIAL SIGNIFICANCE OF HYPERTENSION AND ARTERIOSCLEROSIS

In the study of chronic diseases and particularly their etiology, post-mortem examination disclosed years ago that the lower income group has a higher proportion of diseases such as tuberculosis, syphilis and gastric ulcer. On the other hand the frequency of angina pectoris, diabetes and arteriosclerosis increases with the rise in social status. Ryle<sup>1</sup> concluded from social statistics and detailed clinical histories that mental work and stress and the day-to-day cares of sustained responsibility, rather than deeper emotional conflicts or repressions, are responsible for the high incidence of angina pectoris in the professional class. He felt that we should accept today that social factors such as occupational fatigue and stress, the anxieties which accompany competitive speed and strife and insecurity, together with inadequate opportunity for relaxation and cultural enjoyments, are making their contributions to the rising morbidity and mortality from hypertension and coronary disease. Smirk<sup>2</sup> concedes the importance of environmental factors in the production of hypertension, but goes on to say that the evidence that mechanized and industrial civilizations produce more stress, strain and tension, and thus contribute to hypertension, is largely presumptive, although admittedly it cannot be simply ignored.

As if further to confuse the issue, a study was recently published in which a comparison is made between executives and non-executive employees in the same office building, with regard to incidence of hypertension and arteriosclerosis. Lee and Schneider<sup>3</sup> assumed that executives as a group were burdened with more responsibilities and were exposed to more stress. They were surprised to discover that not only was there no increase in hypertension and arteriosclerotic disease among the executives, but that both conditions were significantly more frequent among comparable groups of male workers in non-executive positions employed in the same building.

This study involved 1171 male executives and 1203 non-executives (of whom 563 were females),

numbers which should allow for reasonably satisfactory statistical evaluation. As possible explanations for their findings the authors suggest that the executives were healthy and therefore were successful in their career, and that their superior training made them realize the value of "escape" valves such as hobbies and recreation. It is obviously impossible to discount the findings by Lee and Schneider, but their explanations are not necessarily the only ones that would explain their results. One could argue that their findings disprove the assumption that executives are burdened with excessive responsibilities and are more exposed to stress.

The unkind thought may occur to one that the executives started out with the right educational background, then worked away in a company quite serene in the knowledge that if they did not make any serious mistakes they would eventually reach the top. One could also argue the reverse and say that people with hypertension and/or arteriosclerosis are frequently of a certain type, temperament or background, which in itself prevents them from achieving success in their careers. Smirk quotes cases in which relief of hypertension is sometimes followed by dramatic disappearance of hostile and aggressive feelings in patients, and states that lesser degrees of reduction of hostility and repression are often observed in the course of successful antihypertensive treatment. The present writer believes that the mere distinction between executives and non-executives is not going to help in the etiological study of hypertension and arteriosclerosis. Incidentally, the large number of executive personnel in a single business building seems excessive, especially when compared with the number of ordinary office workers. One cannot help wondering if the business world is not becoming top-heavy?

Some pertinent comments on the question of stress and its role in the etiology of hypertension and arteriosclerosis were made by Sprague in an editorial in *Circulation* (17: 1, 1958). He thinks that it would be a good thing if more people knew what Selye means by "stress", and reminds us that stress is not new and that Thoreau wrote over 100 years ago that the majority of men lead lives of quiet desperation. Yet these men were not dying of coronary artery disease in 1854! Sprague warns us against etiologic dogmatism in any human disease and we are reminded of the analogy, which is almost banal, that whilst tuberculosis cannot develop in the absence of tuberculosis bacilli, the presence of bacilli does not necessarily produce tuberculosis in every person.

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## Editorial Comments

### MATURING MAN, GROWTH AND AGEING

A recent issue of the *Journal of the American Geriatric Society* (6: 169, 1958) carries a report of a conference held at the Lankenau Hospital, Philadelphia, last October. The theme of the conference was maturing man, growth and ageing. Some points made by speakers are noted below.

McCay discussed the difficulties of research on chronic diseases and emphasized the need for very broad training among scientists in addition to their own specialized field, so that they could understand each other's language and cooperate better. This calls for training in personalities as much as for training in special disciplines.

Much more is known about the best foods than is put into practice, and far too few educated people even among biochemists and nutrition scientists apply their knowledge of good nutrition to themselves.

Outlining present knowledge of cellular mechanism of metabolism, Weinhause pointed to our ignorance of some of the important events in metabolism, such as the localization of the action of hormones. He spoke of the many misconceptions surrounding the relationship between lipoproteins and atherosclerosis, obesity and dietary cholesterol and their importance in atherosclerosis. The difficulty of correlating the incidence of atherosclerotic heart disease with clinical data or dietary habits may in part be due to the lack of a close relationship between coronary or cerebral atherosclerosis so common in the middle-aged and elderly as to be considered a universal affliction. A method for measuring total atherosclerosis is urgently needed. In the present stage of our knowledge there is no justification for going overboard on theories and drastically altering our dietary habits. Until more information is available on the causation of atherosclerosis, a policy of moderation seems the only sensible course to follow.

Waife thinks that the nutritional needs of the elderly in health are basically the same as for younger adults, but that these needs are met in the elderly with greater difficulty. External reasons such as illfitting dentures, food allergy, peptic ulcer, mental disorders, or sociologic factors such as living alone or poverty, make the elderly more prone to dietary deficiency. The middle-aged or elderly should reduce a high fat intake without, however, attributing to this any magic power.

The significance of physical fitness with particular reference to age was discussed by Rodahl. Physical fitness and capacity for physical work is rapidly declining in modern society with the advance of technology and with the disappearance of outdoor activities and sports as part of a nation's culture. The need for physical fitness remains as high as ever, especially in the light of modern global war. According to some studies, it takes very little effort to maintain physical fitness once it has been attained, and this can add tremendously to the capacity of the aged to perform physical work. It is well known that endurance suffers but little with age, although the ability for sudden bursts of extreme activity declines. It is desirable to develop standard tests, the combined results of

which would represent the biologic ageing of the individual. They would take into account intellectual abilities, capacity for physical work and the state of organ functions. With such an index, it would be possible to advise—among other things—a suitable retirement age for a given individual; there is little scientific basis for mandatory retirement at 65.

Problems of retirement were discussed by several psychiatrists as well as by Roberts, who presented a study of a large group of retired employees of the Standard Oil Company. These people were retired because of medical disability and they were compared with another group retired on the basis of service. Roberts concluded that most retired persons had become adjusted to their retirement and were enjoying it. There was no evidence that mortality was any higher among annuitants in the five years following retirement than would be expected according to age.

In a panel on mental health, various questions regarding retirement and emotional maturity were answered. Appel brought up the important question of encouraging motivation in the elderly, so that they may have inner resources to carry them along after retirement or after their children leave them or when they have lost a husband or wife.

Cowdry spoke about significant areas of research in ageing and pointed out that whereas life expectancy at birth has risen by about 20 years since 1900, it has only increased by 1.4-2.7 years at the age of 65. This means that the factors causing death after 65 are still almost the same as they were in 1900. The chief factors are cardiovascular diseases and cancer, and in both there is reasonable hope that some improvement will be forthcoming.

### SUMMER DIARRHÖEA OF INFANCY AND EARLY CHILDHOOD

Acute enteritis or gastro-enteritis of infants and children has not lost its significance as a dread disease in spite of the strides made in its symptomatic treatment. Many etiological agents can produce this disorder, and infection with known micro-organisms of the typhoid-paratyphoid group, dysentery bacilli, etc., was at one time considered to be the chief cause of epidemics. In many epidemics no pathogen could be isolated, and gradually the belief grew that at least in some of them a virus or a group of viruses might be responsible.

The use of tissue cultures in roller tubes for the isolation and study of viruses, though mainly applied to the study of poliomyelitis viruses, made possible the recognition of several other groups of viruses such as the adenoviruses, which are responsible for many cases of minor respiratory infection. From faecal extracts other viruses were isolated which resemble the polioviruses but do not react with their antisera. Since 1950, when the earliest observations on these viruses were made, 13 different antigenic groups of these viruses had been recognized up to 1955, when they were given the name of ECHO viruses.

It is common knowledge that this name stands for "enteric cytopathogenic human orphans", the last word referring to the absence of any association of these viruses with a specific disease, (orphans in search of a disease). Since then the orphan status has undergone some changes, for the ECHO viruses have been isolated in many cases of so-called non-paralytic poliomyelitis and of serous meningitis. Several epidemics of aseptic meningitis in Central Europe in recent years have been found to be due to one or the other of the ECHO viruses. Ramos-Alvarez and Sabin,<sup>1</sup> who have studied enteric viruses for some years, present further evidence that these viruses are not quite the orphans they were thought to be. In a brief review of present knowledge of the enteric viruses, the authors state that at least 46 distinct viruses are known to be at times multiplying in the human intestinal tract; this group, recently termed enteroviruses, is rapidly expanding. In previous studies the authors concentrated on the viral flora of healthy children in Cincinnati and in Mexico. The present study was designed to establish the role of the ECHO viruses and other enteroviruses in summer diarrhoea of infants and children in Cincinnati.

The results obtained in 153 children under 4 years of age with diarrhoea in 1955 and 1956 are compared with those in 100 children of similar age and of the same socio-economic group without diarrhoea at the time of investigation. The specimens for study were obtained by rectal swab for reasons of expediency, although it was recognized that a higher yield would have resulted from stool specimens. In addition serologic and bacteriologic studies were carried out on many of the patients. A large variety of enteroviruses (ECHO, Coxsackie A and B, polioviruses) and a small number of adenoviruses were recovered from some 50% of the children with diarrhoea. The serologic tests indicated that many of the children in whom no virus was recovered had suffered a viral infection. The incidence of ECHO viruses was six times greater in the children with diarrhoea than in those without diarrhoea. Shigella and Salmonella organisms were recovered from only 9% of the children with diarrhoea and from none of the controls, while *Bact. coli* was present in 30% of the diarrhoea group and in 20% of the control group.

The authors conclude that "summer diarrhoeal disease in very young children is not an entity but rather a consequence of transitory infection with a large variety of enteropathogenic viruses and bacteria that are especially prone to produce diarrhea and vomiting as part of the clinical manifestations of infection in very young infants". It is of interest that none of the children studied died, the disease being generally milder among the children from whom only viruses were recovered. This study illustrates vividly the progress that has been made in the study of summer diarrhoea in recent years, thanks mainly to the advances in virus research.

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## CLASSIFICATION AND DIAGNOSIS OF CEREBROVASCULAR DISEASES

With the continuous refinement of diagnostic techniques and the application of some newer forms of treatment, both medical and surgical, the attitude of the physician faced with a patient suffering from one or other manifestation of cerebrovascular disease has undergone considerable changes in the last years. No longer can he treat expectantly even such major catastrophes as strokes, while he has to be aware of much less obvious conditions such as transient ischaemic attacks. Even in the elderly patient with a first cerebral haemorrhage, bleeding from an arterial aneurysm has to be considered in the differential diagnosis and in suitable cases appropriate diagnostic studies must be carried out. Surgical removal of clots is being performed more often with gratifying results.

The ad hoc Committee of the Advisory Council for the National Institute of Neurological Diseases and Blindness of the U.S. Public Health Service has recently published a classification and outline of cerebrovascular diseases.<sup>1</sup> In the foreword Pearce Bailey stresses the importance of cerebrovascular disease, which is the third ranking killer and a foremost crippler of all diseases in the United States. Moreover, he points out that some 175,000 persons died of cerebrovascular lesions in the U.S.A. in 1955 and that of them over 39,000 were in the working age group, 25-64 years. Under the chairmanship of Clark H. Millikan this committee has been working since 1955, trying to clarify thinking in regard to cerebrovascular diseases, and to establish reliable criteria for diagnosis. Although many of the statements made in their report are admittedly only partially correct and will undergo further changes as our knowledge increases, there can be no doubt that this report will promote further research in this field. The cooperative studies at present being carried out augur well for the future. Of great interest are the studies being carried out in various centres and aimed at the evaluation of the treatment of subarachnoid haemorrhage and intracranial aneurysm.

This classification should be particularly helpful in the evaluation of reports on anticoagulant treatment in cerebrovascular disease. McDevitt, Wright and Foley<sup>2</sup> have just published their results with anticoagulants in cerebral thrombosis and in recurrent embolization associated with rheumatic heart disease and myocardial infarction. Their data suggest that the treatment is effective, but they stress the need for meticulous supervision and optimal administration of the anticoagulant. Fisher<sup>3</sup> gives a very detailed description of the various syndromes of insufficiency and occlusion of the cerebral arteries and helpful hints in differential diagnosis. Both papers stress that insufficiency of the basilar artery is a true medical emergency, calling for prompt, effective anticoagulant therapy. Fisher states that his data strongly suggest that anticoagulant therapy abolishes transient ischaemic attacks and prevents or postpones the arrival of a stroke. Similar evidence is also presented in a paper by Siekert and Millikan.<sup>4</sup> Obviously time

has been too short to define with certainty the place which this therapy will occupy in cerebro-vascular disease, particularly when long-term therapy has to be considered, but studies now in progress should provide some definite answers in the not too distant future. If the value of long-term anticoagulant therapy should become accepted, it will be necessary to solve the very considerable problem of practical application of this treatment to the ambulant patient.

W. GROBIN

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#### CHEMOPROPHYLACTIC TREATMENT OF CANCER

Despite the elaborate and increasingly powerful machines used by the radiotherapists, and the "supra-radical" operations made possible by the surgeon's technical skill, there has been a discouragingly small increase in the survival rate in malignant disease.

In recent years interest has grown in the possible role of chemotherapeutic agents in cancer therapy. Triethylene thiophosphoramide (thioTEPA) and triethylene melamine (TEM) have been widely used in the treatment of advanced cancer, and although a permanent cure has not been reported, survival may be prolonged and effective palliation obtained in favourable cases. These compounds are tumoricidal *in vitro*, and the effect is probably a direct one on tumour cells and not just instant alteration in host physiology.

Schell and Hall<sup>1</sup> have reported their experiences with thioTEPA and TEM in 40 patients with advanced malignant disease. A favourable response was obtained in numerous cases of adenocarcinoma, by systemic therapy with thioTEPA or by injection of the substance directly into the tumour mass. Of these, carcinoma of the breast responded most readily. However, malignant ovarian tumours, endometrial carcinoma, and to a lesser degree, adenocarcinoma of the gastro-intestinal tract, definitely responded. There was no objective improvement from either agent when used in squamous cell carcinoma, whether of skin, bronchus or oesophagus, nor did malignant melanoma show a clinical response.

In the search for ways to utilize the known tumoricidal effects of the chemotherapeutic agents, a new concept—one of chemoprophylaxis—has been advanced. The not infrequent appearance of disseminated metastases after cancer surgery suggests that the operation may have either stimulated growth of metastases or caused dissemination of tumour cells. There is also experimental basis for this belief, in that massage of a tumour in animals results in an increased number of tumour cells in the circulating blood and an increase in the number of metastases.

The concept of chemoprophylaxis implies the use of chemotherapeutic agents in the immediate

postoperative period in an attempt to control or prevent the establishment of surgically spread metastases.

This concept prompted Kramer, Eck and Smith<sup>2</sup> to study the effectiveness of thioTEPA in controlling experimentally produced metastatic disease in mice, rats, and rabbits. They injected intravenously a suspension of malignant cells and minute tumour fragments into the animals, and at certain time intervals counted the number of resultant metastases in the lungs. ThioTEPA was given at planned times, before or after inoculation of the tumour cells. It was found to greatly reduce the number of pulmonary metastases from S-91 melanoma (one of the four transplantable tumours used.) Its effectiveness in preventing the establishment of metastases increased to a maximum in the 48 hours after tumour inoculation, and then decreased. This suggests that the treatment of metastatic implants in the immediate postoperative period might indeed have greater success than treatment of established lesions.

The response of the various types of tumours used in the different animals showed considerable variation in their susceptibility to thioTEPA, just as the tumours in humans differed in response. However, when the particular tumour was sensitive to the drug, treatment was highly effective in reducing the number of metastases and, when the dosage was sufficiently large, in preventing metastases. Thus the concept of chemoprophylaxis is experimentally sound.

Obviously, there is a great need for an effective method of evaluating the increasing number of promising chemotherapeutic agents, in an attempt to establish the specific agent for the various tumours which make up the broad spectrum of malignant disease in humans. To meet this challenge, the Committee on Chemotherapy of the U.S. National Advisory Cancer Council has initiated an extensive study of the effects of such agents on the clinical course and survival rates of those operated upon for potentially curable cancer. This project has the co-operation of many large hospitals, which will make possible the statistically significant clinical trial of numerous compounds in a reasonably short time. It is hoped that a further advance will be made in the control of the disease.

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#### CHANGE OF ADDRESS

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**Medical News in brief****KANAMYCIN**

The new Japanese antibiotic, kanamycin, obtained from fermentation products of a *Streptomyces* species, was discussed at the New York Academy of Sciences on July 10 and 11. Its clinical aspects may be summarized as follows. The antibiotic can be used intramuscularly or orally, but absorption is so poor from the gastro-intestinal tract that oral doses of 4 to 8 g. a day are likely only to act by altering the intestinal flora in a manner similar to neomycin, though some success has been reported in some *Salmonella* and *Shigella* infections. Given intramuscularly, its chief interest is in staphylococcal infections; it has been very satisfactory in severe infections by resistant staphylococci. It has also proved useful in acute gonorrhœa and anthrax, as well as some acute and chronic infections of the urinary tract. Chronic urinary infections with *Pseudomonas* or *Proteus* strains resist kanamycin, which also fails in pneumococcal and streptococcal infections. In Japan it has been used in tuberculosis together with PAS, with effects comparable to those obtained by combination of streptomycin and PAS. Kanamycin, neomycin and streptomycin are of course somewhat similar chemically.

Kanamycin has two major toxic effects—on the kidney and on the eighth nerve. Casts may appear in the urine, and some signs of mild impairment of renal function appear in about one quarter of cases. Hearing loss is not uncommon, but vestibular nerve damage is rare. Tinnitus is an early and important sign of eighth nerve damage.

As regards intramuscular dosage, 0.5 to 1 g. in adults at intervals of 6 to 8 hours would seem to be adequate for therapy, though fixed schedules have not been established.

**THE MORTALITY OF RADIOLOGISTS**

There has been some argument in the United States on the question whether an occupational exposure of radiologists to x-rays has a non-specific shortening effect on their lives. Our British colleagues, Court Brown and Doll (*Brit. M. J.*, 2: 181, 1958) have now conducted a study of members of radiological societies in Britain and finally obtained a series of 1377 males whose status was known on January 1, 1957; mortality among them during the 60-year period from 1897 to 1957 was studied. Results show no grounds for pessimism. Although this group included most of the pioneer British radiologists, there was no evidence that occupational exposure to ionizing radiations had caused a detectable non-specific shortening of the expectation of life.

Naturally enough, there was a significant excess of cancer deaths among men entering the practice of radiology before 1921, the year in which organized efforts were first made to protect against excessive exposure. The excess of deaths in these older men was confined to tumours of the skin and pancreas, and possibly leukaemia. There was no excess mortality from cancer among entrants to radiology after 1920.

The authors state that it is clear that under modern working conditions—that is, with provision of and adherence to adequate protective measures—the personnel of medical radiological departments have not run any substantial risk of reduction in expectation of life, or increased mortality from common forms of cancer. They warn, however, against generalizations from such a small sample, since a very small risk would have been difficult to detect in this series.

**BILIARY VESICULAR STASIS**

Of 200 consecutive cases investigated and treated by Ross (*Lancet*, 1: 1356, 1958) for biliary-tract disorder a dyskinesia of the gall-bladder was found in 126, and of them 34 had biliary vesicular stasis. Hypotonic stasis was present in 20 and the remaining 14 were of the hypertonic variety with raised intravesicular pressure. Serial cholecystography with radiography every ten minutes after the fatty meal is required to diagnose stasis, and intravesicular pressure recordings preoperatively will establish the presence of hypertonic stasis. Medical treatment was tried in most cases but failed to relieve the symptoms, which vary from typical biliary colic to vague upper abdominal discomfort or simulate peptic ulcer. The author performed right splanchnicectomy in all 20 cases of hypotonic biliary stasis and vagotomy in the functional type of hypertonic biliary stasis (5 cases). In one case of vesicular stasis associated with recurring pancreatitis, cholecystectomy, vagotomy and sphincterotomy resulted in a complete cure. Hypertonic biliary vesicular stasis due to organic obstruction, such as an infundibulo-colic kink or valve-like abnormalities in the region of the junction between the cystic duct and the gall-bladder, was treated by cholecystectomy with good results. Of all the 34 patients treated surgically only three remained unimproved.

**ORAL TREATMENT OF DIABETES**

Forty diabetic patients were treated by Hall, Crowley and Bloom (*Brit. M. J.*, 2: 71, 1958) with a new oral compound, phenethyl dianamide or N-beta-phenethylformamidinyl iminourea (D.B.I.), which had been found to lower the blood sugar even in eviscerated or alloxan-diabetic animals. The authors found D.B.I. to be an effective hypoglycaemic agent in mild and moderate diabetes, even in the presence of ketonuria, and in some cases which had failed to respond to tolbutamide. It did not relieve ketonuria and its administration was accompanied by gastro-intestinal disturbances in no less than two-thirds of the patients. Nausea, abdominal discomfort, vomiting and diarrhoea were severe enough to necessitate withdrawal of treatment, after which the symptoms subsided quickly. No toxic effects were observed in the blood or in the liver of the patients treated, but the treatment and the period of observation had not extended for more than a few months.

(Continued on advertising page 50)

## REVIEW ARTICLE

### SURGERY OF PULMONARY TUBERCULOSIS

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THE EARLY DEVELOPMENT of thoracic surgery is the history of the early surgical attempts to cure pulmonary tuberculosis by resection. As long ago as 1891, Tuffier of Paris succeeded in removing the apex of a tuberculous lung but the majority of such early excursions into the chest were tragic failures. The main reason for these failures was the inability of the anaesthetists to maintain "negative" pressure in the pleural space. Sauerbruch in 1904 devised a chamber inside which the bodies of the patient and the operating team and the equipment were maintained at a partial vacuum while their heads remained outside the chamber at atmospheric pressure. By this cumbersome method the lung was kept inflated but it awaited the perfection of endotracheal anaesthesia to place thoracic surgery upon a firm foundation. Although this simple method of preventing collapse of the lung was introduced in 1909, the further progress of intrathoracic surgery awaited the more liberal use of blood transfusion and the discovery of antibiotic drugs to combat, respectively, operative shock and postoperative infection which defeated many of the earlier technical successes. Thus it was that in the early 1930's a series of 42 lobectomies was reported with a mortality rate of 64%. It is only fair to the early pioneers to point out that the only patients the physicians turned over to them for surgery were the terminal failures of medical treatment. If the patients survived the actual operation, wound infection, empyema, opening of the bronchus stump and brain abscesses reaped a deadly postoperative harvest. Even as recently as 1940, the mortality of lobectomy was 25% and of pneumonectomy 45%.

While these early attempts at resection were being explored, thoracoplasty, first introduced in 1866, remained the mainstay of the surgical treatment of pulmonary tuberculosis. Sauerbruch and Alexander were responsible for improving the early techniques of thoracoplasty and more recently Holst and Bjork of Sweden have added further improvements to extend the applicability of this valuable procedure. But, as in resection, the mortality rate remained high and in 1934, arrest of tuberculosis after thoracoplasty could not be expected in more than 60% of survivors.

Today, resection for pulmonary tuberculosis can assure 90% cure with an operative mortality rate of about 2%. Thoracoplasty, too, can give a cure

rate of about 90% with a mortality rate of less than 1%. What has made this difference in the short period of 15 years?

A number of factors are responsible for the dramatic change in results of surgical treatment of pulmonary tuberculosis. Firstly, as mentioned above, was the perfection of endotracheal anaesthesia with controlled respiration. Secondly comes the liberal use of blood transfusion, which has become completely safe only in the last 20 years. Thirdly, there is the use of preoperative tests of pulmonary function, so that the operative procedure most suited to the individual patient can be determined. Fourthly, there is the improved surgical technique by which "dissection" lobectomy, pneumonectomy, and segmental resection replaced mass ligature of the hilar structures — a procedure almost inevitably followed by bronchopleural fistula and empyema. Finally, and by far the most important advance in the successful surgical management of the tuberculous patient, is the discovery of drugs which are effective against the tubercle bacillus.

Thus the introduction of streptomycin in 1944, followed by para-aminosalicylic acid (PAS) and isonicotinic acid hydrazide (INAH), cycloserine and other more recent antibiotics, has ushered in a new era in the treatment of pulmonary tuberculosis. These drugs, given in combination and with bed rest, have dramatically improved the pathologic process in the lung so that more limited resections can now be safely undertaken with low mortality and morbidity. It is not beyond the realm of possibility that the surgical treatment of pulmonary tuberculosis will be largely of historical interest in the next decade or so. Meanwhile, there are still numerous patients who can be restored to a useful place in society by surgery.

What are the aims of surgery? The aims of surgery are to bring about permanent arrest of the disease process in the lung while preserving as much function of the uninvolved lung as possible with the least danger to the patient's life or future health. The chosen procedure should ensure the patient an early return to a useful place in society. For example, it is not enough to convert the patient's sputum if he is rendered a bed-ridden "respiratory cripple" as the result of excessive resection of lung tissue. The patient may well wonder "was the operation worth while?" Thus, one of the most important considerations in the surgical management of pulmonary tuberculosis is the careful selection of patients for surgery and the careful selection of the safest and most efficacious surgical procedure for the individual patient. This may often be difficult because many lesions will respond equally well to more than one method of management. It then behoves the surgeon to select the safest procedure for the individual without personal bias for one technique or another.

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## SURGICAL PROCEDURES

The surgical procedures available for the treatment of pulmonary tuberculosis fall into three groups: (1) relaxation procedures, (2) collapse procedures and (3) resectional procedures. The first of these will be discussed briefly, because they are now largely of historical interest.

*Relaxation procedures* include phrenic crush and avulsion, pneumothorax with or without pneumonolysis, and pneumoperitoneum. These rest procedures are now rarely used, having lost most of their usefulness in the primary treatment of pulmonary tuberculosis since it has been shown that antituberculous drugs alone give as good results without the addition of these once-valuable adjuncts. Intrapleural haemorrhage, air embolism, empyema, fibrothorax and bronchopleural fistulae were not uncommon after pneumothorax in particular. Thus exposing the patient to such additional risks is not warranted. Nowadays we use phrenic crush and pneumoperitoneum as temporary methods of space reduction in combination with resectional surgery. Otherwise they have no place in the modern management of pulmonary tuberculosis or in the preparation of a patient for surgery.

*Preoperative management.*—Before discussing the surgical procedures available for the treatment of pulmonary tuberculosis, it is necessary to mention briefly the preoperative preparation of the patient for surgery. When the patient has reached the "target point" which indicates the maximum improvement to be expected from antituberculous drugs and the sanatorium regimen, it must be decided whether or not surgery is indicated. If the indications are present (these will be enumerated later), the operative procedure and its purpose are explained to the patient so that his understanding and co-operation may be obtained. In the doubtful case, pulmonary function is determined before operation so that a thoracoplasty may be substituted for a resection in a borderline patient. Physiotherapy directed at deep breathing exercises and diaphragm control is begun a week before operation to improve pulmonary function preoperatively and to ensure adequate coughing postoperatively, which minimizes atelectasis and promotes rapid re-expansion of the lung. The correction of anaemia, the control of associated diseases, i.e. diabetes, cardiovascular disease, etc., and the precise delineation of the affected lung tissue are necessary to successful surgery. Thus bronchography and planigraphy are performed to locate the diseased portion of the lung accurately. Bronchoscopy is routine, as the presence or absence of tuberculous endobronchitis will determine whether or not a resection is feasible. Sputum cultures and drug resistance studies are valuable, but may or may not influence the surgeon's choice of procedure. Careful, unhurried preoperative preparation and investigation of the patient should never be neglected, as the surgery of pulmonary tuberculosis is never an emergency.

## COLLAPSE PROCEDURES

The aim of these techniques is to produce selective and complete collapse of the diseased part of the lung without undue interference with the function of non-diseased lung tissue. Collapse procedures have stood the test of time, and give a high percentage of good results as regards sputum conversion and cavity closure. The long-term stability of the patient after surgery is well known—a variable we do not yet know in resectional surgery. Three forms of collapse therapy are in present use: (1) standard five-rib one-stage thoracoplasty, (2) osteoplastic thoracoplasty, and (3) plombage procedures.

*Indications for collapse therapy.*—With the more prompt and effective care of the tuberculous patient and with the rebirth of resection, the indications for collapse procedures have become fewer. Generally speaking, however, collapse therapy carries less risk than resection, and gives as high a percentage of arrested cases and so merits more attention than it is at present receiving in most centres.

Where disease is fibrocavernous, bilateral and far advanced, collapse therapy is preferable to resection. The elderly patient who is diabetic or emphysematous or is suffering from cardiovascular disease may not be a safe candidate for resection but may tolerate thoracoplasty without incident. Drug resistance and a positive sputum make resection hazards greater, and active endobronchitis makes resection prohibitive. In such instances collapse therapy is preferable or absolutely necessary, and may be definitive or may be used as a preliminary to later resection. Apical bronchiectasis without stenosis is best treated by a collapse procedure.

*Standard five-rib one-stage thoracoplasty.*—This is the most frequently performed collapse procedure. All of the first, all of the second and progressively shorter portions of the third, fourth and fifth ribs are removed subperiosteally in a one-stage operation under general anaesthesia. The apex of the lung is mobilized extrapleurally, so that the diseased part of the lung is relaxed down to the hilum. The incision is closed without drainage and the mobilized lung stays in its new position by virtue of the extrapleural relaxation and by the space filling with blood and exudate.

The disadvantages of the procedure are several. Immediate postoperative complications are paradoxical respiration as a result of removal of the ribs, so that with inspiration the chest wall moves inward and upon expiration the chest wall moves outward—the reverse of the normal chest wall movements with respiration. This paradox leads to an impaired cough mechanism, atelectasis, severe cardiac embarrassment in the elderly, and the spread of disease. It can be lessened by strapping the chest. Infection may occur in the space left above the collapsed lung. One of the commonest

causes of failure is mediastinal "creep". When this occurs the relaxed lung "creeps" from its relaxed position back up to near its original position. With this upward movement cavities reopen and sputum becomes positive again. Because of these disadvantages of standard thoracoplasty, methods of preventing them have been under study for 50 years.

*Osteoplastic thoracoplasty.*—This procedure is considered by the author to be the collapse procedure of choice in pulmonary tuberculosis, and is used by him almost to the exclusion of all other methods. In the standard five-rib one-stage osteoplastic thoracoplasty, progressively shorter portions of the fifth, fourth, third and second ribs are extra-periosteally resected and the first rib is transected anteriorly and posteriorly but no rib is completely removed. After the usual extrapleural mobilization of the apex of the lung down to the hilum, the fifth, fourth, third and second ribs are sewn by heavy silk to the sixth rib, and the first rib is similarly sewn to the paravertebral tissues posteriorly and to the mediastinal tissues anteriorly. This allows complete and permanent collapse of the diseased portion of the lung to the level of the hilum medially and to below the lowest rib (sixth) posteriorly.

The advantages of the procedure are several. The chest wall is stable (at a new level) so that there can be no paradoxical respiration and cough is effective, atelectasis is rare and cardiovascular difficulties do not occur. Mediastinal "creep" is impossible and deformity is minimal. Since the space is drained for 48 hours, infection is uncommonly rare. The author has performed this procedure in patients up to the age of 65 years with success.

*Plombage* is mentioned only to condemn it. In this procedure an extrafascial mobilization of the portion of lung to be relaxed is carried out and the ribs remain essentially intact. The collapse of the lung is maintained by the insertion of plastic sponges, plastic balls or wax into the space. The incidence of infection is high; migration of these foreign bodies occurs and the patient carries a potential volcano in his chest for the rest of his life. The same effect can be obtained by an osteoplastic thoracoplasty where no foreign bodies are used but the patient's own living ribs are the "plumb". Plombage procedures are fortunately becoming less popular and should be abandoned.

Collapse procedures are still useful, and I use osteoplastic thoracoplasty in most subjects over the age of 55 years when resection is contraindicated and also in the younger patient with advanced bilateral disease. About 15% of patients have this procedure, which is also the technique of choice in a post-resection "tailoring" thoracoplasty. There have been no deaths or serious complications in 50 thoracoplasties at the Saskatoon Sanatorium in the period 1955-1957 (Table I).

#### RESECTION PROCEDURES

The aim of resection is to remove the major foci of residual disease in the lung after the greatest amount of improvement has been obtained by anti-tuberculous drugs and other medical measures. The function of the non-diseased lung is interfered with less than after collapse therapy, which often compresses healthy tissue. After resection there is no fear of residual bronchiectasis remaining as a focus of reactivation or haemoptysis, and no fear of cavities reopening whereas cavities persist in about 5% of thoracoplasties. Also resection ensures the removal of lesions whose nature might be doubtful, i.e. the rounded lesion which may be cancer or tuberculosis.

Although resection is the ideal surgical procedure, it carries a higher mortality and morbidity than thoracoplasty. Part of the reason for the high complication rates reported from some centres is the virtual abandonment of thoracoplasty and the adoption of resection as the universal form of surgical therapy. Such a circumstance immediately implies poor selection and the exposure of a certain number of patients to resection, for which they are not candidates.

*Indications for resection.*—When discussing the indications for resection most surgeons are in agreement that there are certain lesions which do poorly with thoracoplasty and well with resection. The reverse also holds, and in between there is a group of lesions which do equally well with either procedure and in which individual merit must decide the best approach.

Absolute indications for resection include the solid tuberculous lesions—tuberculomas—especially if they are larger than 2 cm. in diameter. When the tuberculous process has healed with stenosis of the bronchus and secondary changes have developed in the lung distally, that portion of the lung is best removed. Thus the destroyed lung or lobe and tuberculous bronchiectasis are indications for resection. Anterior cavities, tension cavities, and lower lobe disease, although uncommon, are best treated by resection. Failed collapse therapy is another absolute indication for surgical resection of the affected lung tissue. Tuberculous empyema is best treated by surgery. This may mean simply a decortication if the underlying lung is healthy, or may mean decortication combined with a resection.

Relative indications for resection include fibrocaseous upper lobe disease and apical bronchiectasis *without* bronchostenosis. These lesions do equally well with thoracoplasty at a much lower risk to the patient. The persistently sputum-positive patient and the one who is drug-resistant are known to have a higher complication rate after resection, and thus are probably best treated by thoracoplasty initially and resection later if conversion is not obtained.

An absolute contraindication to resection is active endobronchitis, particularly when present at

TABLE I.—RESULTS OF THORACOPLASTY AT THE SASKATOON SANATORIUM

Procedure	Number	Age	Sex		Mortality	Morbidity	Failures
			M.	F.			
Osteoplastic . . . . .	27	36 (19-65)	13	14	0	2	1
Standard . . . . .	23	40 (22-63)	11	12	0	4	3

the level at which the bronchus would be transected at operation. In this circumstance, a post-operative bronchopleural fistula is almost inevitable. If active tuberculosis is present in the same or opposite lung, resection is contraindicated. When serious associated diseases are present, e.g. diabetes or heart disease, resection is unduly dangerous whereas thoracoplasty might be quite feasible. Finally, when respiratory reserve is small and resection may leave the patient a respiratory "cripple", operation must not be performed.

*Disadvantages and complications of resection.*—Surgical resection in pulmonary tuberculosis carries a higher mortality and morbidity rate than more established procedures, and the long-term results of resection are not yet known. Large-scale resection is less than 10 years old and it will be at least 15 years before one can be certain of long-term stability. Finally, if the resection is difficult, for technical reasons the surgeon may have to remove more tissue than he anticipated, e.g. a lobe instead of a segment, or perform a pneumonectomy instead of a lobectomy, and thus the patient may be worse off than if he had not had an operation of any kind.

The complications of resection, when they do occur, are serious to life and lung function and often mean a second major operation. The most serious complication is breakdown of the bronchus stump with the development of empyema and a bronchopleural fistula. Such a complication carries a mortality rate in the neighbourhood of 35%. Spread of disease is not uncommon after resection. Persisting pleural space is another common complication after resection. Here the remaining lung does not expand to fill the space formerly filled by the resected lung and if this space is not obliterated by a thoracoplasty, empyema and a secondary bronchopleural fistula may develop. Thus a complicated resection means a second major operation in about 15% of cases. This leads to a further reduction of pulmonary function and defeats the purpose of the initial operation. Resection complications can be kept at a low level if more

thoracoplasties are performed and if more stringent selection of patients for resection is made without denying surgery to those who may be deserving, though poor risks.

*Procedures and techniques.*—The lungs and their lobes are composed of broncho-pulmonary segments, each of which consists of lung tissue supplied by a bronchus, by an artery and by a vein. Thus the technique of pulmonary resection, whether it be of a segment, a lobe or the whole lung, depends upon ligating these vessels individually and then carefully closing the bronchus supplying the lung or portion of lung to be removed. Details of these techniques cannot be discussed here but there are certain important principles common to all resectional procedures.

Contamination of the pleural space must be avoided at all costs or postoperative empyema may develop. Thus extrapleural mobilization of the diseased areas must be used to avoid breaking into cavities or nodules, which invariably contain viable tubercle bacilli even though the sputum is negative. Too, when the bronchus stump is cut across it must be clamped distally and suction used proximally to prevent spill of contaminated or potentially contaminated bronchial secretions into the chest. The bronchus must be carefully transected as short as possible, so that it does not form a sump in which secretions can collect and infection occur with the development of a bronchopleural fistula. Its blood supply must be carefully preserved and the stump covered by vascular mediastinal tissues or preferably pleura. This will ensure better healing and an airtight closure. In segmental resection great care must be taken to avoid transgressing diseased tissue planes, or post-operative air leaks, infection and spread of disease will be common.

After removing the diseased tissue, respecting the principles mentioned above, the surgeon is faced with additional problems. The major of these is rapid elimination of the dead space in the pleural cavity without over-expansion of the remaining lung tissue. This problem is overcome first

TABLE II.—RESULTS OF RESECTION AT THE SASKATOON SANATORIUM

Procedure	Number	Age	Sex		Mortality	Morbidity
			M.	F.		
Segmental resection . . . . .	52	31 (17-54)	22	30	1	11
Lobectomy alone or with segment . . . . .	64	30 (12-58)	28	36	3	15
Pneumonectomy . . . . .	24	33 (9-62)	7	17	1	4

by adequate tube drainage of the pleural space until the lung fills the chest cage. Secondly, careful preoperative and postoperative physiotherapy aids in encouraging re-expansion and preventing atelectasis. Thirdly, if the lung tissue will not fill the remaining space without over-expansion, space-reducing measures such as phrenic crush, pneumoperitoneum or thoracoplasty must accompany the resection, since it is felt that over-expansion predisposes to spread of disease or reinfection. Thus early and complete obliteration of the pleural dead space and removal of bronchial secretions by coughing, by bronchoscopy and, rarely, by tracheotomy are the major postoperative considerations.

Subsequent management varies with the individual. Most of our sanatorium patients are on full activity within one month of resection but remain in hospital for three to nine months and on drugs for at least six months. Return to work can be allowed in six months to one year after operation, depending upon the patient's occupation and social circumstances.

*Results of resectional surgery.*—The results of resection at the Saskatoon Sanatorium in the period 1955-1957 are listed in Table II. It must be remembered that really long-term results are not yet available, but the early results are very encouraging. It is important to realize that figures are meaningless unless one knows the background of the cases operated upon. Thus a surgeon may obtain excellent results by careful selection but by this means deny many deserving patients a possible surgical cure. At our sanatorium, no deserving case is denied surgery unless the operative risk is completely out of line. A 50% mortality rate in salvage surgery may be worth the risk to the otherwise incurable patient when his only alternative is sanatorium residence for the rest of his life, which may be a lingering downhill course to invalidism and an early death. Rehabilitation of such a patient is worth a high risk.

#### SUMMARY AND CONCLUSIONS

The "sanatorium regimen" combined with anti-tuberculous drug therapy has narrowed the indications for surgery in the management of pulmonary tuberculosis. Residual foci of disease can be removed from the lung by resection with a low mortality and morbidity. Resection, however, must not be used to the exclusion of thoracoplasty, which remains a time-tried and valuable operative procedure. Thoracoplasty and resection are complementary, and the best results in the surgical treatment of pulmonary tuberculosis will be obtained by the intelligent combination of these two procedures, especially since the final place of resection is not yet definite. Thoracoplasty remains a valuable procedure and the osteoplastic method in particular will enable cure to be offered to many patients who are not candidates for thoracotomy and resection.

Some of the aspects of the surgery of pulmonary tuberculosis have been presented in this brief review

and the results of surgery at the Saskatoon Sanatorium have been tabulated.

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## GENERAL PRACTICE

### EXAMINATION OF THE DISTURBED CHILD IN GENERAL PRACTICE\*

M. G. MARTIN, M.D.,† *Regina, Sask.*

THIS PAPER DESCRIBES practical methods for the use of the general practitioner in dealing with children in the office. I have worked out a routine during the examination of several hundreds of children seen as out-patients over a period of four years, and I think this routine may be useful to others. My suggestions are particularly for dealing with children aged 4 to 10 but are applicable to most children several years on either side of this range.

It is assumed that the child will be seen separately and that both parents will also be seen. It is important to see the father, especially if the child is a boy.

In work with children, psychological diagnosis is notoriously difficult and unsatisfactory. Diagnoses such as behaviour disorder, neurotic disorder, or habit disorder are not good "working" diagnoses for a variety of reasons. These terms are not specific enough and do not put emphasis on the important point, which is emotional growth. People do not habitually think of children in terms of behaviour, neurosis or habit disorder. The main concern of the child and his parents is his growing up and this process should be included in his diagnosis. Growing up means growing away from the parents and becoming both independent and civilized or fit to live with. This process can be called "differentiation". Disturbances in the process can be called "growth disturbances" and the amount of disturbed emotional growth can be described as mild, moderate, or severe. Using this concept, most of the children seen in the office can be placed in one of the following groups: (1) Normal emotional growth. (2) Growth disturbance: the inhibited or over-dependent child. (3) Growth disturbance: the aggressive or over-assertive child. Either disturbance of emotional growth may be found with any of the other types of disorder, namely, in: (1) The brain-injured child. (2) The deaf child. (3) The retarded child. (4) The autistic child.

I suggest that every practitioner should know something about the actual behaviour in his office of the child described as brain-injured, deaf, defective, or autistic.

\*Presented at the Postgraduate Course in Obstetrics and Paediatrics, Regina General Hospital, April 11, 1958.

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The brain-injured child shows an overactivity, which is described as organic drivenness. He is also very distractable, and under the stress of repeated or too strong stimuli he becomes disorganized in what is called "the catastrophic reaction". The deaf child shows increased visual activity, and he has an odd highpitched voice if the deafness is only partial and some speech has developed. The retarded child may show a disturbance of coordination and gait, his play will not be at an appropriate level for his maturation, and his drawing will be poor in relation to that of other children of his age. The mother may tell you quite accurately at what age level he is performing, especially if she has other children who have been developing at the usual rate. The autistic child is very uncommon and the diagnosis of "early infantile autism" is usually made in only 1 or 2% of cases seen in a child guidance situation. These very interesting children have an intimate relationship with things, but no relationship at all with people. Before the diagnosis of autism is made, they are first diagnosed as retarded and secondly diagnosed as deaf.

Emotional growth is usually disturbed in any of the conditions listed above. The addition of the diagnosis of "growth disturbance" helps by placing emphasis on the personality area where much management of the case will be focused.

#### DETAILED DIAGNOSIS OF DISTURBANCE OF EMOTIONAL GROWTH

To assess the degree of emotional disturbance, one needs a yardstick. The most practical one is based on the following rule: A child aged 4 or over is emotionally healthy if he is (1) reasonably comfortable about himself; (2) reasonably comfortable about others; and (3) able to find satisfaction outside the home.

This means that the child who is emotionally healthy has reasonable self-confidence, is making progress in differentiating himself from his parents, and has sources of satisfaction apart from his parents. Growth disturbance shows itself by inhibition or over-assertion, difficulty in separating from the parents, and difficulty in doing things with the practitioner. There is also an inability to form good relationships with others, either in the neighbourhood or at school.

#### SUGGESTIONS FOR INTERVIEWING

Most inexperienced physicians are quite uneasy with children. This uneasiness takes various forms, depending upon the personality of the physician and also upon his previous experience with children. At times the uneasy physician is excessively hearty with children. At other times he is a rather gruff person addicted to detailed questioning, which, although suitable for some adults, is quite unsuitable for most children. Few physicians are really good in interviews with children—perhaps one doctor in four. Because a physician is skilful in interviewing adults, it does not follow that he is adequate in interviews with children. However, it does appear that most physicians who are good with children are also quite expert in interviewing adults.

Perhaps the main characteristic of the good children's doctor is that he is "childish". I place "childish" in quotes because I really mean flexible and able to meet the child on his own level, both figuratively and literally. This flexibility means intelligent permissiveness plus the ability to be very firm on occasion. In general practice it is sometimes necessary in examining a throat to have the child held quite firmly, after explaining this to him, of course. In interviews to assess the personality of a child, it may occasionally be appropriate to have a locked door or one that gets "stuck". With an occasional over-aggressive child, you may have to set definite limits. You can tell the child that there are two rules in your office: first, the furniture must not be broken and, second, no one gets hurt. (This second rule applies to adult work, too, i.e., if the patient does something that makes you feel less of a doctor this is not good for either you or the patient.) Flexibility also involves acceptance of the fact that sometimes children "beat" you, and quite easily too. At times the child defeats your efforts to size him up and you may have to have him return another day. Sometimes he may dazzle you with weird responses and produce in you what may be called a "boing-boing" response. Occasionally the child interviews *you*, rather than the reverse. I remember one child who said, "What were you before you were a doctor?" I replied, "A little boy just like you" and he responded by saying, "Yes, and before that you were nothing, eh!"

I think that besides flexibility the good "childish" doctor has the ability to have fun with his child patients. Sometimes our very expert interviewers of children actually forget they are interviewing and "working". The child responds to interest, warmth, and flexibility and, of course, the interviewer responds to the child. Part of this response to the child is a "fun" response. You do things *with* children more than you do with adults and the fun experience is an important accompaniment of the child interview. Perhaps guilt about having fun is one reason why so many physicians are not really expert in child interviews.

A final word about technique. The main rule in talking psychologically with either children or adults is what is called "K.M.S." This stands for "keep your mouth shut" but it does not mean actually being silent, of course. It means responding in the so-called non-directive way, for example, "And?", "And then?", or such responses as "Well?", "No!", and "Tell me more!" It also means use of numerous non-verbal responses, that is, gestures of the hands and of the head. But the guiding principle is "K.M.S." Let the child do the talking.

It must be noted, however, that with some children you have to "push" the child during the interview. For example, in the talking phase of the interview to be described, when asking the child to make wishes, you may have to prod him a bit, saying something like, "Go ahead. All the children who come here think of something."

#### PLAY EQUIPMENT FOR THE WAITING ROOM

A certain minimum of play equipment is essential. Adults are able to express themselves with words, but the child needs play equipment for

full expression. (As a matter of fact, much of the child's "play" is really *work*, i.e., he works out his problems of living during his play.) One of the best pieces of waiting-room equipment is an obsolete typewriter on a child-size, child-height table. Children love to pound a typewriter. It may be necessary for the clerical staff to run interference to keep the parents away and give the child an opportunity to bang the machine. (With luck the machine may last two years.) Other waiting-room equipment should include the graphic media (lots of paper, crayons, and pencils), a few toys (dolls, teddy bears, and assorted weapons), and a riding horse on springs.

#### PLAY EQUIPMENT FOR THE OFFICE

The office should have the graphic media, and some thumb tacks for displaying the results of the child's work. In the office a set of dolls representing all the members in a family is very useful. Family relations can also be studied with the use of a set of wild animals, both fierce and friendly. You observe what the dolls or animals do during play and this often gives you a vivid glimpse into life at home, or into the child's inner world, or both.

#### THE INTERVIEW

It is sometimes necessary to vary the approach and to rearrange the order of the phases of the interview to be described below. For example, some children like to draw before talking with you. However, for most children the sequence to be described is quite suitable. This interview has been developed so that the techniques of child psychiatrists can be used to size up the child and to get an idea of the amount of growth disturbance. This can be thought of as the "main thing" about the child and should give sufficient orientation for interpreting the development of the child to the parents. After some practice, this interview should not take longer than 20 to 30 minutes.

There are six phases to the interview: (1) Greeting child and parents. (2) Playing. (3) Talking. (4) Drawing. (5) The presenting problem. (6) The ending.

#### Phase 1.

The first part of the interview is the greeting of the child and the parents in the waiting room. It is of great importance to see how the child separates from his parents, and the reaction of both the child and his parents to this separation. The doctor extends his hand to the child and announces that the two of them are going along to the office "where all the better toys are".

#### Phase 2.

A period of "free" play is especially good for the children who like to explore the office before dealing with you. The child looks around and the doctor makes occasional encouraging remarks. Then as the child plays with the animals or dolls, the doctor puts the play into words, e.g., "The wolf

is sneaking up on the pig", or, "The family is sitting down to dinner".

#### Phase 3.

Ten minutes of talk is next. Usually it is easiest to get started with talk about school. You ask about the pupils there, who his friends are, and who his best friend is (if he has one). Then you discuss the teacher and what is taught. This leads to a discussion of "What are you going to be when you grow up?" Then you ask what he would do with a lot of money if he had to spend it. He can also be asked what he would wish for if he had three wishes. Next you ask him what is the worst thing he can think of in the whole world. This is usually enough talking all in one dose. It should give you a good idea of whom he is identifying with, whom he relates to, and what his main needs are.

#### Phase 4.

He draws for ten minutes while you make comments on his work and discuss it with him. The first drawing should be a "free" one and he should draw anything that comes to his mind. You may have to push a bit to get him to do this. He should draw a person after this, and you may have to ask him to draw the whole person. Then he should draw a picture of the opposite sex. Finally, he should draw a whole family. It is interesting to observe the order in which the family figures are produced and particularly who in the family is next to whom. Note that in all his drawings the figures give the child's picture of *himself* quite accurately. They are also a very reliable indication of intelligence. The child's drawings are an important part of your records and, in addition to being an objective recording of his status, they are useful for comparison with productions he may make later.

#### Phase 5.

The presenting problem is usually left to the last, although sometimes it comes up earlier. In the final part of the interview, you may say, "I understand there has been some trouble about bed-wetting" or whatever the difficulty is. This is followed by the appropriate medical and psychological discussion. Then one moves into the final part of the interview.

#### Phase 6.

This is the ending. It is important to end on a positive note and to let the child know he has done well. You can let him show his skill or his strength in some way. One pleasant way to end the interview is to have him pin up his drawings on a bulletin board while you make suitable laudatory remarks. Some children like to show their drawings to their parents and this is also a healthy sort of ending.

#### INTERPRETING THE CHILD TO THE PARENTS

The parents are anxious to know what has been going on between you and the child, and it is usual

to see the parents together to finish things off, at least for that day. By now you have decided "the main thing" about the child. For example, he may be an inhibited child with over-solicitous parents. It is a useful device to tell the parents that, although the child knows that they love him, he "misinterprets" their solicitousness as lack of confidence in his abilities. You can then discuss how they can change their general handling of him in a more suitable direction. Regardless of your impression of the type of disturbance of emotional growth, in your discussion with the parents the main principle is to help them facilitate independent emotional growth in the child, while at the same time civilizing him and preparing him for living among others.

#### FOLLOW-UP

It is a good idea to have the family back in one month. After greeting them and watching the child's play in the waiting room for a few minutes, you can see the parents separately and discuss the development in the interim. Usually things have been going well. As a matter of fact, many children are much better long *before* they come for their initial appointment. This is probably because the mere fact of the decision to bring the child "for help" has demonstrated to him that his parents have a real interest in him. Follow-up visits are usually quite pleasant and you are usually on the right track in giving support and reassurance to the anxious parents of today.

#### SUMMARY

The diagnosis of disturbed emotional growth in children is considered from the standpoint of the general practitioner. Suggestions are made about interview techniques and play equipment. A specially designed interview for office work with children is described in detail.

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#### ERRATUM

In the July '58 issue (Volume 79, page 128), we erroneously referred to Nacton in the treatment of duodenal ulcer as "a new French drug". May we remind our readers that Nacton was developed in England by the Bencard Research Laboratories, Brockham Park, under the name of compound I.S. 499. This drug is to be released to Canadian physicians in the near future by C. L. Bencard, Weston, Ontario.

## MEDICAL FILMS

CONTINUING the listing of available films on medical and related subjects, we list below additional films. The films are held in the National Medical and Biological Film Library and are distributed by the Canadian Film Institute, 142 Sparks Street, Ottawa, Ontario. The evaluations have been prepared by Canadian specialists in the subjects of the films, under the Medical Committee of the Scientific Division of the Canadian Film Institute, which is headed by Dr. G. H. Ettinger.

#### DISEASE (Pathology, Diagnosis, Treatment)

##### **Therapeutic Uses of Heat and Cold. Part II: Administering Cold Applications—1945; Sound; B & W; 22 minutes.**

Produced for the U.S. Office of Education.

Description.—An instructional-training film, illustrating methods of applying cold as a therapeutic measure, and the underlying principles and physiological results.

Appraisal (1945).—A clear, concise presentation; animation very good; techniques accurate and well carried out. Recommended for professional nurses and suitable for certain lay groups.

Availability.—National Medical and Biological Film Library (\$3.00). Purchase from United World Films, Inc., 1445 Park Avenue, New York 29, N.Y.

##### **Therapy Influencing the Autonomic Nervous System—1952; Sound; Colour; 19 minutes.**

Produced for G. D. Searle & Company.

Description.—An instructional film, presenting the rationale for the use of drugs acting on the autonomic nervous system.

Appraisal (1953).—The approach made to the disturbed physiology of the autonomic nervous system is fairly superficial. Physiology is presented rather superficially but with reasonable clarity. While the film concerns itself with presenting arguments for the use of Banthine (methantheline bromide), it will be found interesting and of some instructive value to medical students in the clinical years and to practitioners. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$3.00). For purchase apply to G. D. Searle & Company, P.O. Box 5110, Chicago 80, Illinois.

##### **Thrombosis and Embolism—1948; Sound; B & W; 18 minutes.**

Produced for F. Hoffmann-LaRoche & Company, Basle, Switzerland.

Description.—An instructional film, demonstrating the pathogenesis and clinical manifestations of venous thrombosis and pulmonary embolism.

Appraisal (1951).—An excellent film, presenting in a clear and interesting fashion the essential pathogenesis of venous thrombosis. Particularly valuable for teaching medical students; of great interest to specialists in medicine, surgery, obstetrics and gynaecology, as well as to all general practitioners. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$3.00). For purchase apply to Medical Audio-Visual Institute, Association of American Medical Colleges, 185 North Wabash Avenue, Chicago 1, Illinois.

##### **Treatment of Criminal Alcoholics—1950; Silent; B & W; 31 minutes.**

Produced by the Institute of Forensic Psychiatry, Department of Police, Copenhagen, Denmark.

Description.—A portrayal of a social experiment in the rehabilitation of criminal alcoholics, within the legal process, by the combined use of Antabuse, psychotherapy and social follow-up.

Appraisal (1952).—While the approach portrayed is not one which could apply in Canada at the present time, since necessary supporting legislation does not exist, the film

has inspirational value in pointing up leads to the handling of criminal alcoholics here. It brings out the importance of careful selection of treatment candidates. This presentation has its shortcomings (errors in English captions, loose editing, etc.), but these are not too important. Recommended for medical and legal audiences—psychiatrists, psychiatric social workers, judges, magistrates, lawyers, etc. Suitable for other professional groups, and for lay groups when presented by a competent authority.

**Availability.**—National Medical and Biological Film Library (\$4.50). For purchase apply to Erik Jacobsen, M.D., Biologiskkemiske Laboratories, A/S Medicinalco, Kobenhavn.

#### Uterine Cancer—The Problem of Early Diagnosis—1951; Sound; Colour; 21 minutes.

Produced for the American Cancer Society and the National Cancer Institute of the U.S. Public Health Service.

**Description.**—An instructional-training film, presenting the problem of uterine cancer and illustrating methods of early diagnosis of cancer of the cervix.

**Appraisal (1952).**—An excellent film, extremely well done. Recommended for medical students in the clinical years, interns, general practitioners and surgeons, and specialists in gynaecology. Suitable for other interested medical audiences—nurses, technicians. *Unsuitable for non-medical audiences.*

**Availability.**—National Medical and Biological Film Library (\$4.00). Purchase from American Cancer Society, Inc., 47 Beaver Street, New York 4, N.Y.

### SOME ASPECTS OF ACCESSIBLE CANCERS Series

The following six films were produced for the U.K. Central Office of Information and the Ministry of Health.

#### Some Aspects of Accessible Cancers, Part I: Skin—1950; Sound; B & W; 29 minutes.

**Description.**—An instructional-training film, presenting some aspects of the diagnosis and treatment of skin cancer.

**Appraisal (1952).**—A very good film to demonstrate and to emphasize points of value in the clinical history of skin cancer, the various types, the importance of biopsy and the means of treatment. While it leans somewhat heavily towards advanced and late stage disease, it should be good to emphasize what may happen if such lesions are neglected or inadequately treated. Recommended for senior medical students, general practitioners, and nurses. Suitable for other medical groups. *Unsuitable for non-medical audiences.*

**Availability.**—National Medical and Biological Film Library (\$3.00). For purchase apply to the Canadian Film Institute, 142 Sparks Street, Ottawa 4, Ontario.

#### Some Aspects of Accessible Cancers, Part II: Lip, Tongue and Mouth—1950; Sound; B & W; 26 minutes.

**Description.**—An instructional-training film, presenting some aspects of the diagnosis and treatment of cancers of the lip, tongue and mouth.

**Appraisal (1952).**—Well executed, but largely applicable only to specialists or postgraduate physicians particularly interested in studying techniques of treatment. For the medical profession in general the film does show what results may be accomplished with certain methods of treatment, but it is not as generally informative as it is particularly instructive to radiation therapists and surgeons. *Unsuitable for non-medical audiences.*

**Availability.**—National Medical and Biological Film Library (\$2.50). For purchase apply to the Canadian Film Institute, 142 Sparks Street, Ottawa 4, Ontario.

#### Some Aspects of Accessible Cancers, Part III: Larynx—1950; Sound; B & W; 25 minutes.

**Description.**—An instructional-training film, presenting some aspects of the diagnosis and treatment of cancer of the larynx.

**Appraisal (1952).**—Very good photography of the individual lesions and of the demonstration of laryngectomy. While the all-round presentation is excellent, the film spends rather too much time on the operative procedure for general use and interest of the medical profession. Sequences on speech training after laryngectomy are good for general medical audiences. *Unsuitable for non-medical audiences.*

**Availability.**—National Medical and Biological Film Library (\$2.50). For purchase apply to the Canadian Film Institute, 142 Sparks Street, Ottawa 4, Ontario.

#### Some Aspects of Accessible Cancers, Part IV: Breast—1950; Sound; B & W; 29 minutes.

**Description.**—An instructional-training film, presenting some aspects of the diagnosis and treatment of cancer of the breast.

**Appraisal (1952).**—An excellent film, but covering points with which specialist groups (radiotherapists and surgeons) are already familiar. Generally informative for the medical profession as a whole, although it uses predominantly late stages of the disease for its clinical examples. Recommended for general practitioners, senior medical students and nurses. *Unsuitable for non-medical audiences.*

**Availability.**—National Medical and Biological Film Library (\$3.00). For purchase apply to the Canadian Film Institute, 142 Sparks Street, Ottawa 4, Ontario.

#### Some Aspects of Accessible Cancers, Part V: Cervix and Uterus—1950; Sound; B & W; 36 minutes.

**Description.**—An instructional-training film, presenting some aspects of the diagnosis and treatment of cancer of the cervix and uterus, stressing the importance of early diagnosis.

**Appraisal (1956).**—Suitable for general practitioners and medical students in the clinical years. This film was made for British medical audiences and some of the techniques and situations are somewhat different from ours. The commendable emphasis on early diagnosis is largely obscured by the detail of actual treatment. *Unsuitable for non-medical audiences.*

**Availability.**—National Medical and Biological Film Library (\$3.00). For purchase apply to the Canadian Film Institute, 142 Sparks Street, Ottawa 4, Ontario.

#### Some Aspects of Accessible Cancers, Part VI: Rectum—1950; Sound; B & W; 25 minutes.

**Description.**—An instructional-training film, designed to emphasize the current status of diagnosis and treatment of carcinoma of the rectum.

**Appraisal (1956).**—Recommended for general practitioners, medical students in the clinical years, and nurses; suitable for other interested medical audiences. A good presentation of the subject. It is not a surgical technique film; its aim is to develop awareness of early symptoms of rectal carcinoma. Its further aim is to emphasize the improved outlook due to modern technique. *Unsuitable for non-medical audiences.*

**Availability.**—National Medical and Biological Film Library (\$2.50). For purchase apply to the Canadian Film Institute, 142 Sparks Street, Ottawa 4, Ontario.

#### Some Aspects of Endocrinology—1936; Silent; B & W; 70 minutes.

Produced at the Medical, Surgical and Neurosurgical Departments, Lahey Clinic, Boston, Mass.

**Description.**—An instructional film, reviewing the major clinical syndromes of endocrine disturbance.

**Appraisal (1947).**—A well-presented and well-coordinated film, of great value to all medical students and practitioners; suitable for any interested medical audience. *Unsuitable for non-medical audiences.*

**Availability.**—National Medical and Biological Film Library (\$6.00). For purchase apply to Worcester Film Corporation, 131 Central Street, Worcester, Mass.

(To be continued)

## Association Notes

### THE CANADIAN MEDICAL RETIREMENT SAVINGS PLAN

This report covers C.M.R.S.P. activities during the quarter year ended August 31, 1958. Moneys which participants have deposited in their special Bank of Montreal savings accounts on or before August 9, 1958, have now been transferred to the Plan. Contributions during this quarter totalled \$255,961.

#### *De-Registration*

You will no doubt remember the endless discussions of last autumn about de-registration of C.M.R.S.P. contracts and the consequent withdrawal of funds. At that time we assured you that participants in C.M.R.S.P. had the same rights and privileges as participants in any other registered retirement savings plan.

We have now received and processed our first request for de-registration. We contacted the office of the Minister of National Revenue to determine the correct procedure and subsequently returned to the participant the amounts owing less the minimum tax applicable (25%).

It is important to realize that this tax which was deducted is the minimum amount and additional taxes may have to be paid by the recipient. These moneys returned are considered to be income in this year and thus the actual tax applicable will be determined by the amount of other income received.

The formula which we used to determine the amount owing to the participant was a return of the current value of his common stock holdings (valued as at the next following quarterly valuation date) and 93.25% of his contributions to the Insured Annuity Plan plus accumulated interest and dividends to date. Of course, tax was deducted from each of these amounts.

#### *Common Stock Fund—Portfolio Changes*

If you compare our current list of stock holdings with that which was published three months ago you will find that during the last quarter we have increased our holdings in most of the issues which we started to purchase six months ago. This represents the completion of our current six-month dollar-averaging program.

We have, additionally, made purchases of nine stocks which were not represented in our last valuation. These are Loblaw Companies Ltd. 'A', Asbestos Corp. Ltd., Canadian Westinghouse, Howard Smith Paper Mills Ltd., Consumers Gas Co., British American Oil Co., Imperial Oil Ltd., McColl-Frontenac Oil Co. Ltd. and Dow Chemical Co.

These purchases have increased the number of different stocks held to 44—thus increasing the diversification of our portfolio. It has also enabled us to obtain representative stocks in the domestic integrated oil industry as well as certain specialized industries in which investment seemed indicated at this time.

#### *Common Stock Fund—Unit Value*

You will note that we have now invested all but a minimum amount of the contributions made to the

Plan. The appreciation in our common stock holdings together with dividends and interest resulted in an increase in the value of each common stock unit from \$10.40 on May 31 to \$11.08 on August 31.

#### *Notice to Non-Participants*

To obtain more information about C.M.R.S.P., please write to The Association office at 150 St. George Street, Toronto. Brochures and other informative literature is available on request. The basic outline of C.M.R.S.P. is simple and extremely flexible, and participation will enable you to obtain tax relief now on savings which you invest to provide retirement income.

If you wish to obtain tax deferment on 1958 contributions, you must file a completed application card prior to December 31, 1958.

#### CANADIAN MEDICAL RETIREMENT SAVINGS PLAN COMMON STOCK FUND

Holdings Valued at Closing Prices, August 31, 1958		
No. of Shares	Description	August 31, 1958 Value
<i>Canadian Stocks:</i>		
1,500	Bank of Montreal . . . . .	\$70,875.00
600	Bank of Nova Scotia . . . . .	36,300.00
1,100	Canadian Bank of Commerce . . . . .	54,450.00
1,000	Royal Bank of Canada . . . . .	67,250.00
900	Toronto-Dominion Bank . . . . .	41,512.50
500	Distillers Corp.—Seagrams Ltd. . . . .	15,000.00
500	Hiram Walker Gooderham & Worts . . . . .	15,625.00
700	Molson's Brewery Class "A" . . . . .	27,300.00
800	Canadian Breweries Ltd. . . . .	26,300.00
800	Building Products Ltd. . . . .	34,500.00
1,000	Canada Cement . . . . .	34,125.00
1,100	Canadian Industries Ltd. . . . .	19,250.00
1,500	Loblaw Companies Ltd. "A" . . . . .	45,750.00
1,600	Simpsons Ltd. . . . .	40,000.00
800	Zellers Ltd. . . . .	24,600.00
100	Aluminium Ltd. . . . .	2,825.00
500	Asbestos Corp. Ltd. . . . .	15,250.00
215	Canadian Westinghouse . . . . .	11,072.50
700	Moore Corporation Ltd. . . . .	52,500.00
1,000	Page-Hersey Tubes . . . . .	33,500.00
175	Dominion Glass Co. . . . .	14,087.50
700	British American Oil Co. Ltd. . . . .	28,700.00
600	Imperial Oil Ltd. . . . .	27,000.00
300	McColl-Frontenac Oil Co. Ltd. . . . .	18,000.00
1,000	Consolidated Paper Corp. Ltd. . . . .	37,250.00
500	Great Lakes Paper Co. Ltd. . . . .	17,250.00
500	Howard Smith Paper Mills Ltd. . . . .	17,000.00
1,000	Powell River Co. Ltd. . . . .	35,500.00
1,000	St. Lawrence Corp. Ltd. . . . .	16,250.00
800	Interprovincial Pipe Lines . . . . .	41,200.00
300	Calgary Power Ltd. . . . .	22,650.00
600	Gatineau Power Co. Ltd. . . . .	22,125.00
900	Shawinigan Water & Power Co. . . . .	25,875.00
500	British Columbia Power Co. . . . .	20,625.00
1,500	Consumers Gas Co. . . . .	48,562.50
1,000	Union Gas of Canada . . . . .	17,750.00
1,000	Bell Telephone Co. . . . .	42,250.00
300	Manufacturers Life Insurance Co. . . . .	76,500.00
450	Confederation Life Association . . . . .	73,743.75
Total Canadian Stocks . . . . .		\$1,270,303.75
<i>United States Stocks:</i>		
500	Dow Chemical . . . . .	32,062.50
150	E. I. Dupont de Nemours . . . . .	29,175.00
600	General Electric Co. . . . .	38,175.00
300	Owens Illinois Glass . . . . .	21,675.00
700	Standard Oil of New Jersey . . . . .	39,025.00
		\$160,112.50

(Continued on page 507)





# C.M.A. - B.M.A. Meeting, Edinburgh, July 20 - 24, 1959

## FOR YOUR WIFE

The ladies of the City of Edinburgh Division of the British Medical Association are looking forward to your visit during the C.M.A. and B.M.A. Meeting in July 1959. You might like to know something of the arrangements we are making for your stay here.

First of all there will be a club for men and women, situated in the historic Music Hall and Assembly Rooms, George Street. The men and women from Canada will all register here and we hope that it will be the centre of the social side of the meeting. In this spacious building there will be a restaurant, lounges and writing rooms. Various functions will be held in the ballroom and dancing will be arranged most evenings, including some Scottish Country Dancing. Excursions and expeditions to places of interest will start from the club.

There will also be a children's centre in the Women's Students Union, George Square. Excursions for children, whether accompanied by their mothers or not, will be arranged from here. Smaller children may be left at the centre for parts of the day to enable their mothers to be free for some hours.

As July in Scotland is rarely very hot, it is suggested that Canadian women include the following in their packing:

- A top coat.
- A woollen suit with a choice of sweater or blouse.
- A raincoat or umbrella.
- A silk or cotton frock for warm days.
- A long or short evening gown.
- A fur or woollen stole.
- A cocktail dress.
- A pair of comfortable low-heeled walking shoes.

If it is desired to send a bag in advance it may be addressed to:

B.M.A. SCOTTISH HOUSE,  
7 Drumsheugh Gardens,  
Edinburgh, Scotland,

and should be clearly labelled with the owner's name.

ELIZABETH A. BOXENDINE  
JOAN K. SUTHERLAND  
Conveners, Ladies' Functions



(Continued from page 504)

Canadian Equivalent:	2 3/4% discount on U.S. Dollar
	160,112.50 x 97.25 = 155,709.41
<i>Value of Stocks:</i>	
Total Canadian Stocks.....	\$1,270,303.75
Canadian Equivalent of U.S. Stocks.....	155,709.41
Total Value of Stocks.....	\$1,426,013.16
Cash.....	3,651.36
Dividends declared but unpaid on stocks selling ex dividend.....	4,137.03
	\$1,433,801.55
<i>Less: Administration Expense Allowance 1/8% quarterly.....</i>	1,792.25
<i>Net Value of Fund.....</i>	<b>\$1,432,009.30</b>

On the basis of 129,237.079 outstanding units, the unit value is \$11.08. Contributions made to the Common Stock Fund during the three months prior to August 9 will purchase units at this rate.

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#### HAVE YOU FORWARDED YOUR APPLICATION TO C.M.R.S.P.?

Last year 1800 C.M.A. members applied for membership in the Canadian Medical Retirement Savings Plan. Individual contributions varied between \$300 and \$2500, with the average participant contributing about \$1100 during 1957.

Certain tax advantages accrued to these participants as they were able to deduct their contributions from earned income for taxation purposes. In addition, their moneys were invested and interest and appreciation have substantially increased the invested amounts.

During this year the Insured Annuity Plan has credited interest at the rate of 4.5% per annum. During the same period the unit value of the Common Stock Fund has increased from \$10.00 to \$11.08. While these results, of course, cannot be guaranteed for the future, they indicate the care and attention which these investments receive.

If you are contemplating participation in C.M.R.S.P.—ACT NOW. Information and application cards may be obtained from the C.M.A. office—150 St. George Street, Toronto. Non-participants who wish to obtain tax deferment for 1958 must file an application card with the Plan prior to December 31, 1958. Contributions for the 1958 taxation period may be paid into the Plan at any time up to February 9, 1959.

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## PUBLIC HEALTH

### EPIDEMIC OR UNUSUAL COMMUNICABLE DISEASES IN CANADA

During the week ending August 2, 1958, the Epidemiology Division of the Department of National Health and Welfare, Ottawa, received the following surveillance reports of epidemic or unusual communicable diseases.

#### POLIOMYELITIS

NEWFOUNDLAND.—Dr. Aod McDermott, Chief Medical Health Officer, St. John's, has reported a case of paralytic

poliomyelitis in a 2½-year-old boy who had received three injections of Salk vaccine.

#### SHIGELLOSIS

NOVA SCOTIA.—Dr. H. B. Colford, Director of Child and Maternal Health and Communicable Disease Control, has forwarded the following reports:

*Camp Aldershot, N.S.*—Eleven cases of bacillary dysentery; *Shigella sonnei* has been isolated from the stools of five cases.

#### INFLUENZA

*Halifax County, N.S.*—A report has been received from Dr. J. R. Cameron, Divisional Medical Health Officer, that 200-300 cases of an influenza-like disease have occurred in the past month.

ALBERTA.—Dr. E. S. Orford Smith, Director, Division of Local Health Services, has forwarded a report relating to an outbreak of epidemic influenza-like disease in the area of Hanna. It has affected about 60% of the population and is mostly prevalent in children. The symptomatology is rather suggestive of epidemic pleurodynia—onset rapid, fever, chills, substernal pain increasing and spreading up and outward, intercostal myalgia causing some breathing difficulty.

#### BOTULISM

BRITISH COLUMBIA.—Dr. W. B. Laing, Medical Officer, Skeena Health Unit, reports one case of botulism at Port Edward. The source of infection is believed to be salmon egg "caviar". A sample of the "caviar" has been sent to Dr. C. E. Dolman for bacteriology.

#### MENINGITIS

*New Westminster, B.C.*—Dr. E. Wyld, Medical Officer of Health, Simon Fraser Health Unit, has reported one case of meningitis, caused by *Haemophilus influenzae*, in an infant. The patient was hospitalized at the Royal Columbia, following a fulminating onset. The diagnosis was established by autopsy and recovery of the organism.

#### PERTUSSIS

*Vernon, B.C.*—Dr. Duncan Black, Medical Officer of Health, South Central Health Unit, has reported 70-100 cases of whooping cough-like illness in Vernon, Lumby and surrounding district. The disease is severe in its symptomatology, with marked whooping, vomiting and in some cases syncope. Mainly infants and preschool children are affected.

INDIAN AND NORTHERN HEALTH SERVICES.—Dr. P. E. Moore, Director, Indian and Northern Health Services, and Dr. J. S. Willis of the Northern Health Services, have forwarded the following reports received from Dr. W. S. Barclay, Regional Superintendent, Pacific Region, Indian Health Services:

*Tofino, B.C.*—An outbreak of whooping cough has affected mostly young babies on Abousaht and Clayuquot reserves. Two babies were brought to Tofino Hospital from Hot-springs Cove and one died within 24 hours.

*Fort Babine, B.C.*—Ten per cent of the local population is suffering from whooping cough.

#### INFECTIOUS HEPATITIS

*Nasco Reserve, near Quesnel, B.C.*—Dr. J. D. Galbraith, Coqualeetza Zone, has reported three cases of infectious hepatitis. Dr. G. E. Stoker is investigating the outbreak.

#### MEASLES

*Repulse Bay, N.W.T.*—Dr. N. Gillison, Northern Health Services, has received information that the majority of the population in the area is thought to be affected. So far about 80 cases have been diagnosed and 3 deaths have been reported (one at childbirth and two premature infants shortly after birth). It is presumed that the epidemic is subsiding.

## LETTER TO THE EDITOR

## PSYCHOPROPHYLAXIS OF LABOUR

To the Editor:

The writer of the editorial on psychoprophylaxis (*Canad. M. A. J.*, 79: 124, 1958) demonstrated a certain understanding, apparently not experienced by the obstetricians, when he left the last word in his article to the wife who was overheard to remark, "I've just been listening to a lot of men talking something they know nothing about." While I agree with the lady, and believe it is time women began to speak up on this subject which concerns them so deeply, I do feel our comments should be more critically constructive.

My authority to speak starts with the fact that I am female, married, a mother. Further, I conduct prenatal classes for my physician husband's patients. Thus, while I am forced to admit that my experience has been brief in terms of years, it has been more inclusive than that of most obstetricians, being personal, social, as well as medical in nature.

I am led to ask at the outset, what is the purpose of the new term "psychoprophylaxis"? Aside from being a polysyllabic tongue-twister designed to confuse the layman, I cannot see that it is any more descriptive than "education for childbirth" or "natural childbirth", depending upon whether the emphasis is to be on the method or the result. On the other hand, if we define psychoprophylaxis as "prevention of psychological problems of labour", why did not one of the obstetricians at Montreal (*Canad. M. A. J.*, 79: 206, 1958) discuss at length the psychological benefits of the method? What magic "in measurable obstetrical units" do they expect from mere truth? The real arguments for education of mothers are purely psychological! Obstetricians should be satisfied with the fact that it does no obstetrical harm.

By trying to reduce the aesthetic value of natural childbirth to statistics and theories, several of the speakers at the convention demonstrated a male, or at least scientific intelligence totally incompatible with psychoprophylaxis.

For example, I am compelled to contradict Bell of London almost entirely as regards his Fears of Pregnant Women. (1) Expectant mothers still fear death. Statistically, this fear should be negligible, as he claims, but how often do we meet the "died-in-childbirth" theme in stories, movies, etc.? Moreover, he neglects to mention fear of an abnormal or stillborn child, a great source of apprehension for many women. (2) On the other hand, women do not fear pain, per se. It is the unknown factor combined with the spectre of pain that produces tension: how much longer? how much worse? These are the important questions. (3) Bell shows some insight by including fear of the unknown. But, if he admits that women are afraid of what they do not understand, why does he deliberately exclude the explanation of labour and delivery in his prenatal classes? He might as well shout "Labour is too horrible to tell you about!" Often fear of childbirth comes from having heard others' descriptions of the "ordeal", but just as often it comes from having heard Nothing.

Similarly, the apparent agreement that husbands should not be allowed in the delivery room is born of motives other than concern for the total welfare of the mothers. The desire to have the husband present is by no means universal at this point, but once joy and exaltation replace the degrading operative atmosphere in the delivery rooms, both parents will want to share the experience. What better way to create the "atmosphere of confidence and security" urged by Vellay of Paris than to unmask the secrecy of the delivery room, and welcome the father to a new and highly spiritual union with his wife and baby?

Several of the men at Montreal deplored the current campaign for natural childbirth. Let me remind them that for centuries the public concept of human reproduction has been shrouded in superstition, ignorance, prudery, practically any degrading attitude you care to mention. As little as fifteen years ago a pregnant woman on the streets was met with raised eyebrows.

It is the opinion of this mother, and her husband, that natural childbirth is the greatest sociological force ever to be released. Future generations will prove this as they analyze their decrease in juvenile delinquency and crime, lowered divorce rate, empty "rest homes". I hope this statement is provocative, Doctor, for I leave you to consider it!

Binbrook, Ontario,  
August 10, 1958.

HELEN CARY BELL

## ABSTRACTS from current literature

## MEDICINE

**Effect of Smoking on the Cardiovascular System of Man.**  
G. M. ROTH AND R. M. SHICK: *Circulation*, 17: 443, 1958.

In normal subjects smoking or the injection of nicotine produces transient vascular effects on the heart and blood vessels. Apparently tobacco angina or tobacco heart is a clinical entity. Abnormal vascular responses after smoking in normal subjects may be due to hypersensitivity to nicotine, such as occurs in tobacco heart, or to the effect of nicotine on a vascular system demonstrated to be hyperreactive by the cold pressor test. Tobacco is one of the most prominent contributing factors in *thromboangiitis obliterans*, as thromboangiitis is rarely found in non-smokers. The question as to whether or not the effects of smoking are due to sudden increased work of the heart or constriction of the coronary artery has stimulated a great amount of research. There is evidence to support both theories. The findings of abnormal ballistocardiograms before and after smoking in the offspring of hypertensive parents and after smoking in the offspring of parents with coronary heart disease are highly important. Statistically, coronary artery disease seems to occur more frequently and at an earlier age in the person who smokes much than in the nonsmoker. Likewise, the mortality rate is higher among younger persons with coronary disease who are smokers than among those who are nonsmokers.

S. J. SHANE

**Coronary Insufficiency Associated with Oral Administration of Gall-bladder Dye.**

N. D. LITTMAN AND F. I. MARCUS: *New England J. Med.*, 258: 1248, 1958.

Four cases of myocardial infarction, three terminating fatally, followed the oral administration of cholecystographic media. All four patients were known to have arteriosclerotic heart disease. Iodoaliphionic acid (Priodax) was the medium used in two cases, iodo-panoic acid (Telepaque) being employed in the remaining two. While the onset of myocardial infarction could have conceivably been coincidental in all four cases, the authors feel there is probably a causal relation, probably through stimulation of vagal activity by the ingested cholecystographic medium. They recommend administration of atropine to all patients with arteriosclerotic heart disease undergoing oral cholecystography, in order to counteract increased vagal stimulation.

NORMAN S. SKINNER

**Blood Supply of the Human Interventricular Septum.**

T. N. JAMES AND G. E. BURCH: *Circulation*, 17: 391, 1958.

The blood supply of the human interventricular septum was studied in 43 normal hearts prepared by injection of the vessels with vinylite, followed by corrosion of the tissues with concentrated hydrochloric acid. The major blood supply of the ventricular septum was found to be derived from diagonally penetrating arteries entering from the left anterior descending coronary artery. Branches from the posterior descending coronary artery supplied only a small zone of the ventricular septum near the posterior interventricular sulcus and the region of the atrioventricular node. The interventricular septum is an important site of collateral circulatory channels in the human heart. S. J. SHANE

**Normal Kidneys and Retinæ after 35 Years of Diabetes.**

K. M. WEST: *Ann. Int. Med.*, 47: 1256, 1957.

A patient had had diabetes mellitus for 29 years, i.e. from May or June of 1919. An examination carried out in May 1955 revealed no sign of retinopathy. Studies of renal function produced normal results. Roentgenograms of the extremities demonstrated no signs of arterial calcification. Neurologic examination, including sensory examination of the extremities, was negative. On the other hand, roentgenographic signs of calcification of the aorta were present, and the electrocardiogram showed left bundle-branch block.

The patient had never received long-acting insulin. During the years from 1919 to 1924 the disease was controlled by a rigid diet which consisted chiefly of meat and green vegetables. Glycosuria was persistently present, and the patient's body weight remained 50 lb. below the previous figure. Insulin was used intermittently during the period from 1924 to 1932, with a resulting increase in body weight of less than 20 lb.

During the periods of insulin therapy, the content of carbohydrate in the diet was augmented by between 120 and 220 g. per day. Despite the restriction of carbohydrate, glycosuria occurred whenever insulin was omitted. From 1932, unmodified insulin was used three times a day (in dosages amounting to an average of 40 units per day), and the content of carbohydrate in the diet varied between 170 and 200 g. per day. Urinalysis was carried out regularly between one and four times a day from 1932; glycosuria was rare, and

when it did occur, it disappeared promptly on increasing the dose of insulin or reducing the carbohydrate in the diet.

Re-examination of the retinæ in April 1956—i.e. after about 37 years of diabetes—was negative. The patient feels well and is active.

S. J. SHANE

**Wegener's Granulomatosis.**

G. B. GORDON *et al.*: *Ann. Int. Med.*, 47: 1260, 1957.

The association of necrotizing granulomatous lesions with giant cells in the respiratory tract, with an extensive arteritis and focal glomerulitis, was first noted by Klinger in 1931 and described by Wegener in 1939 as a distinct clinical-pathologic entity. In this paper, there is reported a classical case of this disease. The differentiation of this case from other forms of generalized arteritis is discussed. The patient was a white woman, aged 38 years, with a history of five weeks of severe nasal obstruction, including the nasal mucous membranes and the sinuses. This was associated with fever, general debility and diffuse abdominal pain. There was no response to penicillin therapy. The abnormal findings included hypochromic anaemia, polymorphonuclear leukocytosis, elevation of urea nitrogen in the blood, albuminuria, and microscopic haematuria. The electrocardiogram revealed inversion of the T wave in leads 2, AVF, V4 and V5. The chest radiograph showed disseminated linear infiltrations throughout the left lung field. The fever and nasal obstruction improved during the first week of hospitalization, but progressive anaemia and uraemia supervened. The patient died on the 11th day of hospitalization.

There were extensive necrotizing granulomas, with giant cells in association with angiitis, most marked in the lungs, and focal glomerulonephritis.

Wegener's granulomatosis may be distinguished from other forms of generalized arteritis such as periarteritis nodosa, hypersensitivity angiitis, and allergic angiitis with granulomatosis. Clinically Wegener's granulomatosis is characterized by a predominant involvement of the respiratory tract, by terminal uraemia, and by the absence of clinical allergy or hypertension. Tissue biopsies frequently render an early diagnosis possible.

S. J. SHANE

**Relationship of the P Wave to Left Atrial Volume in Rheumatic Heart Disease with Mitral Stenosis.**

L. A. SOLOFF AND J. ZATUCHNI: *Am. J. M. Sc.*, 235: 290, 1958.

The relationship of the character of the P wave to the volume of the left atrium was studied in 20 persons with rheumatic heart disease, mitral stenosis and normal sinus rhythm. Notching of the P wave was the commonest abnormality and high amplitude the least frequent. Notching, amplitude or duration of the P wave could not be correlated with degree of left atrial enlargement. Electric axis of P was commonly semivertical, occasionally vertical and rarely horizontal. A QR complex in lead V<sub>1</sub> is not related to degree of left atrial enlargement but is associated with marked pulmonary hypertension, right atrial enlargement and increased heart size. There is a tendency for the large left atrium to be associated with rightward deviation of P, but left atrial volume is best correlated, although poorly, with deviation of QRS to the right associated with an almost equal deviation of P to the right.

S. J. SHANE

**Clinical Features of Infectious Mononucleosis (in German).**

G. CLEMENCION AND I. KIEBSCH: *Deutsche med. Wochenschr.*, 83: 257, 1958.

This is a review of symptoms, signs and laboratory findings in 121 patients with infectious mononucleosis seen during the decade 1947-1957. The frequency of splenomegaly (in 86.7% of cases) and of liver involvement is stressed; the authors consider that there is damage to the liver parenchyma even though this is not usually demonstrable on liver biopsy.

The serological test (Paul-Bunnell) was positive in two-thirds of cases, over 70% had a white cell count well over 10,000 (34.5% over 15,000), and in over 80% there was a lymphocytosis of 50% and over.

The most important symptoms were sore throat, anorexia, headache, constipation, vomiting and nausea, in that order of frequency.

W. GROBIN

**The Concept of "Masquerading" Bundle-Branch Block: An Electrocardiographic-Pathologic Correlation.**

P. N. UNGER *et al.*: *Circulation*, 17: 397, 1958.

The electrocardiographic complex referred to as "masquerading bundle-branch block", consisting of the pattern of left bundle-branch block (LBBB) in the limb leads and right bundle-branch block (RBBB) in the unipolar precordial leads, has generated considerable speculation and interest relating to possible mechanisms responsible for its production.

Two cases having the features of "masquerading" bundle-branch block were subjected to careful histologic study of the entire heart, including the conduction system. In each instance, bilateral bundle-branch lesions of considerable intensity, which did not completely disrupt the continuity of the branches, were demonstrated. In each case there was extensive destruction of the interventricular septum and the free walls of the left ventricle, and marked bilateral ventricular hypertrophy. In both cases the vascular changes in the heart were those of diffuse arteriosclerosis. It is suggested that this electrocardiographic complex is the result of partial bilateral bundle-branch block. It is further suggested that the concept of "masquerading" bundle-branch block be discarded.

S. J. SHANE

**The Retina in Hypertensive Disease.**

S. A. SHELBYRE: *Ann. Int. Med.*, 47: 1154, 1957.

Results are presented of studies, extending over the past 27 years, with regard to retinal lesions associated with hypertensive disease, with special reference to arteriolar alterations and their significance in the hypertensive picture. The alterations in question are illustrated by drawings executed under the direction and supervision of the author himself. This work commenced at the Peter Bent Brigham Hospital in Boston with the demonstration that oedema of the disk in hypertension was readily associated with elevated pressure in the spinal fluid. This finding was confirmed subsequently and independently by a study carried out by Pickering in England. The problem of nicking at the arteriovenous crossing was studied for many years and it was determined that the recognition of various grades of arteriovenous nicking is important, because these lesions differ greatly in their significance, depending on whether they are minimal or fully developed. The fully developed form of the lesion is infrequently seen except in cases of hypertensive

disease, and in 95% of these cases it is associated with cardiomegaly. The minimal form of the lesion occurs in nonhypertensive patients but its association with hypertensive disease naturally is much more common. Its association with cardiac enlargement is much less general. A study of certain cases of early arteriovenous nicking was undertaken, and it was demonstrated clearly that the transition of the early form to the fully developed form of the lesion occupies a long period of time. This fact was suspected but it had never been previously demonstrated. The recognition of the significance of arteriolar narrowing, of segmental constriction, and of arteriolar thromboses is discussed with reference to a series of drawings. The relation is emphasized between these lesions and the high-diastolic types of hypertension. It is interesting to note that, while segmental constrictions, etc., are manifestations of a high-diastolic type of hypertension, arteriovenous nicking is generally associated with a more chronic type of hypertension of moderate grades of severity. Nevertheless, not infrequently these lesions occur simultaneously in the same patient.

S. J. SHANE

**SURGERY****Surgical Treatment of Partial Anomalous Pulmonary Venous Connections Involving Both Lungs with Interatrial Communication.**

F. H. ELLIS, JR. *et al.*: *Proc. Staff Meet. Mayo Clin.*, 33: 65, 1958.

Anomalies of part of the pulmonary venous return are more common than the total form, and it has been estimated that 0.7% of routine necropsies disclosed anomalies of this type. Of all the cases of partial anomalous pulmonary venous connection so far reported, both lungs have been involved in only two. In usual instances the right lung is involved twice as often as the left. The commonest sites of anomalous connection for the right pulmonary veins are the superior vena cava and the right atrium. The left innominate vein and the coronary sinus are frequent locations of partial anomalous connection involving the left lung. The inferior vena cava, the azygos vein, and the left subclavian vein are less common sites for reception of anomalous pulmonary veins. Patients with total anomalous pulmonary venous connection almost always have signs and symptoms referable to the heart. On the other hand, patients with partial anomalous pulmonary venous connection may be asymptomatic. Usually when more than 50% of the pulmonary venous return is abnormally connected, symptoms are present. The clinical signs are variable, but usually there is a systolic murmur of variable intensity in the second or third left intercostal space, sometimes accompanied by a thrill. The electrocardiogram may show right axis deviation, right ventricular dilatation with or without hypertrophy, or right bundle-branch block. Roentgenography is of considerable help if an abnormal pulmonary vein can be seen, but this unfortunately is not usually the case. Anomalous connection of part of the pulmonary veins may be characterized by the large size of the pulmonary artery and its branches if the pulmonary blood flow is significantly increased above normal. Roentgenoscopically these vessels are seen to pulsate actively. Angiocardiography may also help in delineating the course of an anomalously connected pulmonary vein. Haemodynamically this malformation is similar to an ordinary atrial septal defect with a

left-to-right shunt. Accurate diagnosis may be extremely difficult by ordinary right heart catheterization. However, considerable assistance may be obtained by comparison of the recorded patterns of dilution of an indicator dye during its initial circulation after injection into the pulmonary vein or veins entered by the catheter, into the venae cavae and into the left and right main and lobar pulmonary arteries.

In partial anomalous pulmonary venous connection, involvement of both lungs is rare. This report presents two instances of such malformation. Both patients were operated on with employment of extracorporeal circulation. A complete repair was effected in each case, although only one patient survived the operative procedure.

S. J. SHANE

**Evaluation of Arterial Reconstruction and Sympathectomy by Direct Stimulation Ergometry.**

E. A. EDWARDS: *A.M.A. Arch. Surg.*, 76: 200, 1958.

An attempt to measure changes in muscle function objectively after operations for the relief of claudication is described. The test involved the lifting of a weight on the foot by stimulation of the calf muscles and the recording of tracings of muscle contractions.

Patients who had recovered spontaneously from acute arterial occlusion showed recovery of muscle, confirming clinical experience. Patients who had had successful reconstructive operations did not recover calf muscle power perfectly, the peak increase being 256% of the preoperative levels occurring at 10 months. Five out of 17 limbs showed a consistent fall in muscle power. This was correlated with diffuse disease and imminent arterial closure in some and with high ischaemic neuritis in others.

Patients who had had sympathectomy showed an average peak of 264% of preoperative muscle power at 13 months. Of 31 limbs, 17 showed a diminution in muscle power. This seemed due to progressive arterial occlusion in some. Results could not be correlated with preoperative pulse levels or postoperative changes in pedal pulses.

In both groups the measured performance correlated poorly with the patient's own estimate of his walking ability.

BURNS PLEWES

**Essential Problems in the Treatment of Patients with Strangulated Hernia (in Russian).**

V. I. STRUTCHKOV: *Sovet. med.*, 1: 20, 1958.

This is a review and analysis of the mortality of acute surgical conditions with particular emphasis on strangulated hernia by the surgeon-in-chief of the Ministry of Health of the U.S.S.R. The mortality rate for acute appendicitis had dropped from 5% in 1940 to 1% in 1949, and to 0.17% in 1955. Perforation of duodenal ulcer caused 25% mortality in 1940, 13.3% in 1949 and 4.2% in 1955. In acute bowel obstruction the corresponding figures are 40%, 24.6% and 10.4% and in strangulated hernia 10%, 4.9% and 2.3% for the years 1940, 1949 and 1955. In contrast to the significant drop in mortality from all other acute surgical diseases, strangulated hernia did not show the same degree of improvement in mortality statistics; in fact, the mortality has remained unchanged for the past three years. The author analyzed the records of 35,000 cases of strangulated and 180,000 cases of uncomplicated hernia in order to find out the reasons for this lack of progress.

Cause of death is considered under two headings: (1) immediate cause, i.e. pathological changes leading to death, and (2) causes creating unfavourable circumstances for proper treatment and recovery. Of all patients 75% died of peritonitis from leaking of bowel contents through the suture line or from infection through a devitalized bowel incorrectly judged viable at the time of operation; 11% died from thromboembolic disease complicating their postoperative period in the presence of cardiovascular disease. Postoperative pneumonia caused 7% of all the deaths. Shock caused death only rarely, and that only in strangulated diaphragmatic hernia.

Among the causes which created unfavourable circumstances for recovery are delay in admission to hospital, undue prolongation of diagnostic investigation, belatedness of operation, failure to estimate the extent of toxicity, and disturbance of vital functions in the patient. All these factors are briefly discussed and the following recommendations made in conclusion: (1) Educational effort should be directed towards informing the population about the dangers of neglecting a hernia, and the advantages of operation to prevent strangulation. (2) Standards of district doctors must be raised so as to improve their management of strangulated hernia at home. (3) Early operation should be performed in all cases where strangulated hernia cannot be excluded. (4) Preoperative management of strangulated hernia should be the same as in bowel obstruction. (5) More radical resection is needed of bowel which may be devitalized and may contribute to infection or postoperative paralytic ileus if not resected. (6) Postoperative management should be the same as in bowel obstruction.

W. GROBIN

**Surgery in Hæmophilia.**

G. J. FRAENKEL: *J. Roy. Coll. Surgeons, Edinburgh*, 3: 54, 1957.

The coagulation defect in hæmophilia is only fairly specific. Past and family history, excessive bruising, and joint defects provide a lead towards the recognition of the disease, but a certain diagnosis requires examination by an expert. A prolonged coagulation time with a normal bleeding time is not adequate evidence. In hæmophilia, anti-hæmophilic globulin is lacking in the plasma and an animal anti-hæmophilic globulin has been prepared. Operations on hæmophilic patients are uneventful at the time but the bleeding continues gently for days, weeks and even months.

Avoidable operations should not be performed. Deformities due to hæmarthroses are best corrected by careful gradual traction and wedged plasters. Patients who have been bleeding from the tongue, pharynx or tooth are better treated for threatened asphyxia by intubation rather than tracheotomy. Incisions for haemorrhages into soft tissues have also proved dangerous, even when a collection of blood has become a chronic cyst of years' duration. Acute appendicitis in the hæmophilic is best treated conservatively, especially since the diagnosis is often wrong and the signs and symptoms are due to retroperitoneal haemorrhage. Gastrointestinal haemorrhage as from a peptic ulcer should not be considered surgical. Haematuria, though common, is one of the least serious forms of bleeding. Operations on hæmophilic patients should be avoided at almost any cost, but when unavoidable only two methods of securing haemostasis are available: pressure and administration of anti-hæmophilic globulin (A.H.G.).

A.H.G. may be administered by massive transfusion with fresh blood or fresh plasma or fresh-frozen plasma, and these are effective for 24 hours.

A.H.G. extracts from human blood require large amounts of blood for their production and are usually of low potency. A.H.G. from animals is antigenic, often toxic, and is used only for special indications and with great caution. It is not released from the Oxford centre because of its dangers.

Skin grafting by autografts is a useful tool. Meticulous haemostasis by ligature and suture is important, and absorbable materials like gelatin sponge are valuable. But unavoidable surgical operations must be preceded by some method of raising the anti-haemophilic globulin level, preferably with a cooperating haematological team.

BURNS PLEWES

## OBSTETRICS AND GYNÄCOLOGY

### Surgical Treatment of Cancer of the Cervix.

A. BRUNSCHWIG AND W. DANIEL: *Am. J. Obst. & Gynec.*, 75: 875, 1958.

The record is presented of a program devised and followed up to evaluate the accomplishments of modern surgery alone as primary treatment for cancer of the cervix. This evaluation is based on a consecutive series of 348 patients with cancer of the cervix in stages I, II, III and IV admitted to the out-patient clinic, ward and private services. Recurrent cases are excluded. The results of surgery for radioresistant cervix cancers and for recurrences after radiation have been reported elsewhere.

Modern surgery is an effective method of treating cancer of the cervix. Under favourable circumstances and with skilled operators, patients may be given an 80% chance for "cure" if the disease is localized to the cervix. The over-all 5-year salvage among 348 patients with cancer of the cervix in stages I, II, III and IV was 55%. Even if pelvic lymph node metastases are present, appropriate modern surgical attack can offer an appreciable chance for "cure" (26% among 99 patients in all stages in this series).

It is apparently impossible to state categorically whether radiation or modern surgery is the better primary treatment for cancer of the cervix. Which method is employed will depend upon the facilities available in each locality as to radiation therapy equipment and talent on the one hand, and surgical interest and talent on the other hand. Both methods of therapy may be highly effective in favourable circumstances.

It is important that a "base line" be obtained to show what modern surgery alone can accomplish in a series of minimally selected patients. This article is a progress report of an attempt to secure such fundamental data.

ROSS MITCHELL

## PÄDIATRICS

### Enteropathogenic Viruses and Bacteria. Role in Summer Diarrhoeal Diseases of Infancy and Early Childhood.

M. RAMOS-ALVAREZ AND A. B. SABIN: *J. A. M. A.*, 167: 147, 1958.

A test group of 153 children with summer diarrhoea were compared with a matched control group of 100 children without diarrhoea as to the results of bacteriological and virological examination of rectal swabs. In addition, acute and convalescent phase sera were obtained from many of the patients. The number of

enteric viruses recovered from the rectal swabs of the test group was 2.5 times the number recovered from the control group. Viruses of the ECHO group were recovered six times more often from the children with diarrhoea, and it was only to these viruses that a statistically significant etiological role could be assigned. It appears that summer diarrhoea of very young children is not an entity but rather a consequence of transitory infections with a large variety of bacterial and viral pathogens.

S. J. SHANE

## RADIOLOGY

### Roentgenologic Criteria for Appraising the Human Back as an Economic Asset or Liability

G. W. HENRY, I. J. LARSEN AND S. F. STEWART: *Am. J. Roentgenol.*, 79: 658, 1958.

Backache is an important cause of medical disability, especially in industries where heavy manual labour is employed. For this reason many industries carry out a careful roentgenologic examination of the lower back as part of their pre-employment examination. The most important areas of the back are the lower two lumbar and the first sacral segments. Abnormalities in this region are highly important, particularly in applicants under the age of 30.

The authors suggest the following general criteria in the estimation of an applicant's suitability for heavy muscular work (although admitting the need of modification through sensible medical judgment in any individual case):

*Group A.*—Fit for any type of work. Among the abnormalities in the lower spine which are felt to be of no clinical importance are the presence of a limbus body, four or six lumbar vertebrae, united epiphysis of the pars articularis, mild asymmetry of the zygapophyseal facets and transitional lumbosacral vertebrae with solid fusion of one or both transverse processes.

*Group B.*—Fit for employment as a labourer but not repetitious or continued heavy work affecting the low back. Defects which place applicants in this group are appreciable asymmetry of the zygapophyseal joints, moderate spina bifida occulta, Schmorl's nodules at the L4 or L5 level, and moderate degenerative changes in the upper lumbar spine or small vertebral body spurs in lower areas.

*Group C.*—Not fit for employment where heavy lifting or heavy muscular work is necessary. This includes applicants with spondylolysis or spondylolisthesis, with narrowing of the intervertebral disk space at L4 and L5 or between L5 and S1, those with transitional lumbosacral vertebrae transverse process articulations with the ala of the sacrum, or those with marked hypertrophic changes in the upper lumbar spine or moderate changes in the lower area. Other abnormalities which place applicants in this group are: wedged vertebra, haemangioma or neoplasm of any sort, extensive spina bifida occulta, combinations of minor changes, and evidence of previous spinal surgery, previous spine infection or previous myelography. Old Marie-Strümpell spondylitis, significant osteoporosis and, of course, any gross congenital anomaly are included in the criteria of this group.

Roentgenologic examination of the lower spine has proven its value in the selection of employees for heavy muscular work, but it must be technically good and adequate in scope. The authors employ five projections routinely and frequently require as many more in individual cases.

NORMAN S. SKINNER

## THERAPEUTICS

### Cushing's Syndrome Produced by Normal Replacement Doses of Cortisone in a Patient with Defective Mechanism for Steroid Degradation.

J. E. HOWARD AND C. J. MIGEON: *Am. J. M. Sc.*, 235: 387, 1958.

A case report is presented in which panhypopituitarism followed hypophyseal operation for acromegaly. Under replacement treatment with androgen and cortisone 25 mg. per day orally, the patient developed many of the manifestations of hyperadrenocorticism (Cushing's syndrome). Thyroid therapy had not been given because there were no clinical evidences of hypothyroidism, despite the fact that radioiodine uptake and protein-bound iodine were in the hypothyroid range. Liver function was also abnormal; there was elevated serum globulin, positive cephalin flocculation and thymol turbidity and bromsulfalein retention.

With thyroid replacement (2 grains U.S.P. preparation per day) and maintenance of androgen and cortisone dosage, all manifestations of hyperadrenocorticism disappeared, before liver function tests returned to normal. No cause for the abnormal liver function was discerned.

The disappearance rate of injected hydrocortisone was studied in the patient and, before treatment with thyroid, corresponded to rates previously reported in patients with myxoedema and with hepatic cirrhosis. Even when all evidence of hyperadrenocorticism had disappeared, hydrocortisone did not disappear at a normal rate in this patient.

The authors express the opinion that, in evaluating syndromes due to excessive quantities of a normal hormone, the factors of disposal of hormone should be given serious consideration. Where disposal mechanisms are interfered with, a normal quantity of a hormone may become a physiologically excessive quantity.

S. J. SHANE

### Intravenous Drug Therapy of Stokes-Adams Disease: Effects of Sympathomimetic Amines on Ventricular Rhythmicity and Atrioventricular Conductions.

P. M. ZOLL *et al.*: *Circulation*, 17: 325, 1958.

The effects of intravenously administered epinephrine, isoproterenol, levarterenol, phenylephrine, and sodium lactate on ventricular rhythmicity and atrioventricular conduction were studied in 83 drug trials in 21 patients with Stokes-Adams disease. Epinephrine and isoproterenol in dilute solutions were equally effective in arousing ventricular pacemakers in patients without intrinsic ventricular activity while they were being kept alive by prolonged external electric cardiac stimulation. Both drugs were also effective in accelerating and maintaining ventricular activity. Minor cardiac toxicity (excessive ventricular acceleration above 50 beats per minute or premature ventricular beats), occurring equally with both drugs, was an indication to slow or stop drug administration; major cardiac toxicity (persistent ventricular tachycardia or fibrillation) did not occur. In addition, both epinephrine and isoproterenol occasionally produced transient increase in atrioventricular conduction. Levarterenol, in addition to its marked vasopressor action, also affected ventricular rhythmicity and atrioventricular conduction whereas phenylephrine had only a vasopressor effect. Differences of this nature may prove important in the selection of a sympathomimetic amine for a particular

cardiovascular effect. Limited observations of sodium lactate showed it to be less effective than epinephrine and isoproterenol in arousing and accelerating ventricular pacemakers.

S. J. SHANE

### Penicillin Anaphylaxis in a Patient on Steroid Therapy.

L. BERNSTEIN AND A. LUSTBERG: *Ann. Int. Med.*, 47: 1276, 1957.

This report concerns the first known and published case of penicillin anaphylaxis in a patient under long-term treatment with steroids. For four years, a white woman, aged 44 years, had received daily doses of prednisolone for the treatment of chronic rheumatoid arthritis. On numerous occasions she had received procaine penicillin without incident. There was a history of sporadic attacks of urticaria. She developed acute otitis media, and was treated with 600,000 units of procaine penicillin. An almost-fatal anaphylactic reaction occurred within 30 seconds after the intramuscular injection of penicillin. The resuscitation of the patient followed almost immediately on the administration of adrenaline and other supportive measures. A specimen of serum obtained the day after the anaphylactic reaction contained antibodies of the passive-transfer type. Although the presently available steroid compounds are potent members of our anti-allergic armamentarium, this case demonstrates that they are not capable of inhibiting anaphylaxis of unusual intensity.

S. J. SHANE

## PATHOLOGY

### Atherostatic and Lipophage-Stimulating Effects of Manuronate.

P. CONSTANTINIDES AND P. SAUNDERS: *A.M.A. Arch. Path.*, 65: 499, 1958.

This study from the Anatomy Department, University of British Columbia Faculty of Medicine, was designed to investigate the properties of a sulfated polymannuronide, Manuronate. It had previously been shown that a non anticoagulant sulfated polymannuronide given to animals in the presence of a high cholesterol intake was able to prevent the development of cholesterol atherosclerosis and arrest its progress if already established. It also suppressed lipæmia and stimulated lipid phagocytosis in reticuloendothelial tissues and kidneys. Manuronate, an anticoagulant sulfated polymannuronide, has similar properties, as the present experiments on rabbits show. It depressed the elevation of blood lipids caused by high cholesterol (1%) diet as effectively as did cholesterol withdrawal. Being commercially available and relatively inexpensive, it is considered by the authors a suitable compound for further experimental and clinical studies in the field of atherosclerosis. The investigators believe that their experiments have proved conclusively that the foam-cell reaction produced by Manuronate is due to lipid, coming from exogenous fat removed from the blood by macrophages. This undesirable reaction is apparently due to too rapid clearing of the lipids from the blood stream, and it could be considerably reduced in intensity when the cholesterol load alone or the Manuronate dosage alone was reduced. It disappeared altogether when both cholesterol intake was somewhat reduced and Manuronate dosage was decreased, without losing the anti-lipæmic effect of the compound.

W. GROBIN

## OBITUARIES

**DR. JOHN S. BIGHAM** died suddenly at his home in the village of Drumbo, Ont., on July 18. He had practised in Drumbo for the past 17 years, previous to which he was at Innerkip for some years. He was a graduate of the University of Toronto Medical School.

Dr. Bigham is survived by his widow and one son.

**DR. VINCENT KILLORAN** died on August 3, in Honolulu, Hawaii. He was born in Hastings, Ont., and was educated in Norwood and Peterborough, receiving his degree in medicine from the University of Toronto in 1928. After serving his internship at Hamilton General Hospital, he did postgraduate work at Buffalo General and Children's Hospitals. In 1948, he left his practice in Sandusky, Ohio, and moved to Florida because of ill health. He was a member of the American Medical Association, and also a member of the honorary medical society, Alpha Omega Alpha. At the time of his death he was taking a vacation in Honolulu.

Dr. Killoran is survived by his widow and three children.

**DR. JOHN H. PALMER**, 62, died at the Royal Victoria Hospital, Montreal, on August 9. He was born in Bedeque, P.E.I., and received his early education at Gagetown, N.B., and Mount Allison University. He entered McGill University in 1913, but interrupted his medical studies to serve in the First World War. He went overseas with the No. 3 Canadian General Hospital (McGill) and was later transferred to the No. 2 Canadian Field Ambulance. He then became surgeon probationer to the RCNVR, where he served until the end of the war. In 1921, Dr. Palmer graduated in medicine from McGill University, interned at the Royal Victoria Hospital, and then went to Trail, B.C., where he practised for a number of years. He did postgraduate work in London and Vienna in 1930-31. From 1934-36, he worked with Sir John Parkinson in cardiology, and was appointed to the attending staff of the Royal Victoria Hospital, Montreal. In 1940, he went overseas with the Canadian General Hospital as a major. He was promoted later to lieutenant-colonel and served in the Italian campaign. After some months, he was promoted to colonel and appointed consultant for the Canadian Corps in Italy. His returned to England in 1945. After the war, he returned to his post at the Royal Victoria Hospital, Montreal, where he remained as head of the department of cardiology until his death.

Dr. Palmer is survived by his widow and three daughters.

## FORTHCOMING MEETINGS

### CANADA

**ONTARIO PUBLIC HEALTH ASSOCIATION**, Ninth Annual Meeting, Toronto, Ont. (Dr. R. B. Sutherland, Secretary-Treasurer, O.P.H.A., 150 College St., Toronto 5, Ont.) September 29-October 1, 1958.

### UNITED STATES

**THE ACADEMY OF PSYCHOSOMATIC MEDICINE**, Fifth Annual Meeting, New York, N.Y. (Dr. Bertram B. Moss, 55 E. Washington, Suite 1035, Chicago 2, Ill.) October 9-11, 1958.

**INTER-SOCIETY CYTOLOGY COUNCIL**, Annual Scientific Meeting. Hotel Statler, New York, N.Y. (Dr. Paul F. Fletcher, Secretary, 634 North Grand Avenue, St. Louis 3, Missouri.) November 13-15, 1958.

**INTERNATIONAL ANESTHESIA RESEARCH SOCIETY**, 33rd Congress, Miami Beach, Florida. (Dr. A. William Friend, Executive Secretary, Wade Park Manor, East 107 and Park Lane, Cleveland 6, Ohio.) April 20-23, 1959.

### OTHER COUNTRIES

**SIXTH PAN AMERICAN CONGRESS OF RADIOLOGY**, Lima, Peru. (Dr. Manuel Lesende, Secretary, Inter-American College of Radiology, Tucuman 1516, Buenos Aires, Argentina.) November 2-7, 1958.

**INTERNATIONAL CONGRESS OF PLASTIC SURGERY**, London, England. (Mr. David Matthews, Secretary General, 152 Harley Street, London W.1, England.) July 13-17, 1959.

## PROVINCIAL NEWS

### BRITISH COLUMBIA

This writer must begin by confessing to a bad mistake made in the news from this province, published in the July 15 number of the Journal.

He made the statement that the business tax exacted from professional men in certain cities and municipalities in B.C. (lawyers, doctors, etc.) had been disallowed by the B.C. Supreme Court. This, unfortunately, is not the case, and the statement was based on a misunderstanding of the press reports, which stated, quite correctly, that the B.C. College of Physicians and Surgeons, the Bar Association corresponding to the College, the Professional Engineers' Association, and so on, had been adjudged not liable to this tax. The writer took this to mean the members of these associations, but it actually meant merely the Associations, as incorporated bodies, doing business as such.

We regret extremely that this mistake should have been made, as it may lead to confusion and misunderstanding. We have not changed our mind about the equity or otherwise of these taxes, but they are still legally enforceable.

For some time past the question of nursing homes, and the necessity of regulating these, has been a live question in this province, and especially in Vancouver.

Miss Jean Howarth, a reporter and columnist of the *Vancouver Province* newspaper, conducted a very searching inquiry into nursing homes, the process consuming several months. She found and reported a great many defects, which are disconcerting to say the least, in many so-called nursing homes—patients underfed, dirty, and uncomfortably lacking proper medical and nursing care, and so on. Her reports created considerable public unease.

The Greater Vancouver Health League, a Community Chest agency having on its Board members of the medical, nursing and legal professions, has been working on this question for four years, and has worked out suggested legislation, to ensure licensing and control of all "nursing homes" and other places caring for the aged and infirm. It is a very thorough document.

covering nearly every conceivable part of the question. It has been presented to the Hon. Eric Martin, Minister of Health and Welfare, who promised that he and his deputies would examine the report and Suggested Act, with a view to setting up means by which the problems can be met satisfactorily.

The question of hospital sweepstakes has recently been brought to the fore, this time with the editorial blessing and support of some of the newspapers, notably the *Vancouver Province*.

In an editorial, this paper strongly advocates the legalizing of hospital sweepstakes in Canada "to help the functioning of our hospitals". Its main arguments are: (1) that the hospitals need the money; (2) that the people want them; (3) that Canadian money goes abroad to buy sweep tickets, and might better be spent in Canada; (4) that the Government sanctions gambling, in the form of horse races, and participates in the profits; and that (5) legalized hospital sweepstakes seem to be the lesser of two evils.

These are all very specious and plausible arguments, but we hope, for the sake of the hospitals themselves, if for no worthier reason, that this never comes about. The only people that we can see profiting by it are the promoters. From what we have been able to gather, the hospitals ultimately lose in many ways, and only a small part of the money obtained goes to them.

The beaches of Vancouver, one of its greatest assets, are, according to latest reports, in danger of being closed, on account of the pollution by sewage and other measures, of the water that bathes them. Reports of contamination have been made by the Provincial Department of Health which indicate that this has reached, or will soon reach, a danger point. When one realizes that on a hot summer day many thousands of people may visit one or other of our twelve beaches, one can see the seriousness of the situation.

Plans for sewage disposal have been suggested, but so far no definite decision has been made, and it is hoped that this will soon be done. Meanwhile, the speed with which the public reacts to the suggestion of danger may be seen by the facts that on the next day after the report appeared in the press, the attendance at the beaches fell to a mere fraction of the usual number.

Plans for the Annual Meeting of the Canadian Medical Association, B.C. Division, in October, are far advanced. The meeting will be held at Kelowna, and a very strong list of speakers and clinicians has been arranged.

The U.B.C. Board of Governors has under consideration, for early action, the construction of a Medical Centre at the university, to include a hospital, which would be a combined teaching and research hospital. Chancellor A. E. Grauer, at a meeting of the Governors with the Hon. Eric Martin, Minister of Health and Welfare for B.C., gave a full account of this project.

J. H. MACDERMOT

## MANITOBA

A Special Convocation of the University of Manitoba has been arranged in conjunction with the Annual

Meeting of the Manitoba Medical Association, in order to commemorate the 75th anniversary of the Faculty of Medicine of the University of Manitoba and the 50th anniversary of the Manitoba Medical Association. This meeting is to take place from October 6-10 inclusive, 1958. The sessions will be held in the Royal Alexandra Hotel, and in the Auditorium of the Medical College.

The guest speakers include two former teachers, J. C. B. Grant and William Boyd; also distinguished graduates Donald H. Patterson, Charles Code, E. Harry Botterell, Brian Bird, David B. Stewart, E. Perry McCullagh, Frank B. Walsh and Kenneth Johnston. On October 8 the Alumni Association of Winnipeg General Hospital will hold a reception and dinner. Dr. Arthur F. Van-Wart, President of the Canadian Medical Association, will be the speaker at a luncheon on October 9, and on the evening of that day there will be class reunions. A dinner and dance on October 10 will wind up the meeting. The new wing of the Winnipeg General Hospital will have its scientific opening during the week.

Dr. C. Kirk Osterland has been awarded a National Research Council fellowship at the department of physiology and medical research of the University of Manitoba.

The Manitoba Heart Foundation has given the following grants to the University of Manitoba: \$5868 to support research under the direction of Drs. H. G. T. Strawbridge and Georgina Hogg of the department of pathology; \$15,000 to the department of pharmacology and therapeutics for research under the direction of Dr. M. Nickerson; \$7120 to assist in the research program in the department of surgery under the supervision of Dr. Walter Zingg.

The annual meeting of the Winnipeg Clinic Research Institute was held on June 26. The Neil John Maclean Memorial Award for Medical Research was presented, together with \$250 donated by Dr. P. H. T. Thorlakson, to Dr. T. K. Goodhand. The paper submitted for the award was "The Use of Isolated Ileal Loops for Total Replacement of the Ureter". Dr. W. E. Abbott assisted him in the research. The General Practitioner Postgraduate Award was given to Dr. Stephen Toni of Altona. The Research Institute made a grant of \$250 at the request of Professor H. Medovy for expenses involved in research by Dr. J. C. Haworth on "Some Aspects of Carbohydrate Metabolism in Newborn Babies". The Institute selected Mr. John Peters as recipient of the undergraduate scholarship. Mr. Peters will work during the summer with Professor J. C. Wilt on staphylococcal infections.

Drs. Kenneth C. Finkel, William May and Frederick P. Waugh have joined the staff of the Winnipeg Clinic in the respective fields of paediatrics, ophthalmology and internal medicine.

Dr. A. A. Earn, who has been taking postgraduate work in the University of Sheffield, has begun practice in obstetrics and gynaecology at 394 Graham Avenue, Winnipeg.

With Stewart McLean, the new Minister of Education, at the controls of a bulldozer, ground was broken on July 9 for the new \$1,135,000 dental building immediately north of the Medical College. Interested spectators were Dr. H. H. Saunderson, president of the University, Dr. J. W. Neilson, dean of the faculty of dentistry, and Mr. W. J. Condo, comptroller of the University. The building will be ready for the fall classes of 1959.

Leonard A. Moroz of Winnipeg, a third-year medical student of the University of Manitoba, has been awarded a \$500 scholarship for research and clinical training in allergic diseases by the Allergy Foundation of America. He is one of 22 students from medical schools in the United States and Canada to receive such an award. He will work on a study of penicillin sensitivity under Dr. T. W. Fyles and Dr. Peter Warner, professor of bacteriology at the University.

Dr. Norman C. Hill has opened an office for the practice of neurosurgery at 421 Medical Arts Building, Winnipeg.

A wing at Brandon Tuberculosis Sanatorium is being used as a rehabilitation centre for Indian and Eskimo patients. The purpose of this Brandon program is to assess the capabilities and needs of the prospective rehabilitants and to provide social training and a better understanding of occupational responsibility.

The annual report of the Sanatorium Board of Manitoba shows that the death rate from tuberculosis is 5.4 per 100,000 population for non-Indians and 90.4 for Indians, with an overall rate of 7.5. Sixty-five per cent of those dying were over the age of 50 and 39% of all tuberculosis deaths were in persons over 70 in the ratio of five males to one female. Twenty per cent of all discharged patients had some form of major chest surgery.

ROSS MITCHELL

## ONTARIO

Dr. H. Gerald Wagar, formerly Senior Physician, State Hospital, Foxboro, Massachusetts, has accepted an appointment as psychiatrist on the full-time staff of the Institute of Psychotherapy, Kingston, Ontario.

## QUEBEC

The work of the committees of the Montreal Medico-Chirurgical Society and of those responsible for the success of the program in the coming year is in full swing. There will be some changes introduced. For some years now all Society scientific meetings were held on Fridays and this will be changed to Mondays. In addition, three of the nine Society meetings will be preceded by a buffet supper at 6.30 p.m., with the regular meeting at 7.30 p.m. This will permit members to come to the meetings right after office hours and thereby, it is hoped, increase attendance. An outstanding program has been planned for the coming year, which includes many excellent speakers.

We are terribly shocked at the news of the very untimely passing of the recently appointed Honorary Secretary of the Montreal Medico-Chirurgical Society,

Dr. William S. Bauld. This is another example of the hazards that lurk on our roads today. The tragedy occurred as a result of a head-on collision near Sussex, N.B., in which Dr. Bauld, his wife Marion and two of his sons were killed. The two remaining children, a son and a daughter, also sustained very serious injury. This is a great loss to the Society as well as to our whole profession in Canada. Dr. Bauld was the associate director of the Department of Metabolism, Montreal General Hospital, as well as assistant professor of medicine at McGill University. Since his coming to Montreal in 1954, he had established himself as an outstanding medical scientist, a teacher and administrator.

The Montreal General Hospital recently announced the appointment of three of our divisional members to the rank of Senior Physicians. They are: Dr. Gordon A. Copping, Gerald W. Halpenny and Stuart R. Townsend. All three doctors hold the post of Assistant Professor at McGill University. All three are active-members in our Division and well known locally as well as nationally. Dr. Halpenny is also the Honorary Secretary of our Division as well as Honorary Treasurer of the Society. Our sincere congratulations upon their promotions.

The Jewish General Hospital of Montreal has announced the appointment of an assistant pathologist, Dr. W. Arthur Harland, to the staff. Dr. Harland is a graduate of the Queen's University of Belfast and he completed his postgraduate training in the United States at Emory and Columbia Universities. Since 1955 he has been pathologist and director of laboratories at St. Joseph's Hospital in Chatham, Ont.

Dr. Paul Dagenais-Pérusse, chief of the paediatric department of Ste-Jeanne d'Arc Hospital, has been elected President of the Montreal Paediatric Society for the coming year. Other officers elected from the executive committee of the society are Dr. Jean Piete, Vice-president, and Dr. Guy Girardin, Secretary-treasurer.

A. H. NEUFELD.

## NEW BRUNSWICK

Dr. J. Clarence Bourque has been appointed Director of the Psychiatric Clinic at Edmundston. This new clinic is one of several provided by the Provincial Department of Health. Dr. Bourque has had several years of special studies following nine years in general practice. For four years he represented Madawaska in the Provincial Legislature.

Dr. J. A. Melanson, Chief Medical Officer of the Department of Health, New Brunswick, reported to the N.B. Medical Society Annual Meeting that during the past year the hospital accommodation in the province had been improved by the completion of the Forrest Hill Rehabilitation Centre at Fredericton with facilities for 20 in-patients. St. Joseph's Hospital and the new addition to the Saint John General Hospital will be ready for occupancy this year. An addition to the Hôtel-Dieu Hospital at Campbellton will provide 70 beds, and one floor of the new hospital at Chatham is already in use.

In the near future Soldiers Memorial Hospital at Campbellton will add 70 beds. Sackville Memorial

Hospital will build a new 28-bed wing, and the Miramichi Hospital at Newcastle a 30-bed addition. The Victoria Public Hospital at Fredericton will build a new wing; the number of beds has not yet been determined. In Saint John the Evangeline Hospital has begun a new building to contain 13 beds and other clinical departments.

Dr. Conrad Drolet, Medical Superintendent of the Provincial Hospital at Campbellton, has completed an extension course in hospital organization and management in Toronto.

Dr. John B. Bewick and Dr. Edward Walter have established practices in Saint John and both have been appointed to the associate staff of the Saint John General Hospital.

Dr. C. J. Alexander has been appointed to the Department of Pathology and Dr. L. R. G. Rustige to the Department of Anesthesia at the Saint John General Hospital.

A. S. KIRKLAND

## BOOK REVIEWS

**INTRODUCTION TO CLINICAL ENDOCRINOLOGY.**  
A. Stuart Mason, Senior Lecturer, Medical Unit, The London Hospital, England. 192 pp. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1957. \$5.50.

To the medical student endocrinology is one of the most fascinating of the medical specialties. But there is often a wide gap between fascination and understanding. To acquire a working knowledge of the diagnostic and therapeutic advances that have taken place in this subject in recent years, the student must first learn well the physiological principles upon which the practice of endocrinology is based.

Endocrine physiology is presented with admirable clarity in this small book. The introductory chapter deals with the general structure of hormones, the mechanism of their action and the regulation of their secretion. In the following chapters the individual hormones of various endocrine glands are presented in more detail. The pathological and clinical features of endocrine disease are discussed briefly but adequately. The endocrine aspects of general medical disease are emphasized throughout.

The text is a pleasure to read. The absence of illustrations is not as much of a drawback as one might expect. As the author points out, pictures of full-blown typical cases tend to retard the student's appreciation of the great importance of individual variation in the manifestations of endocrine disease.

This book should enjoy a well deserved popularity with medical students and practitioners.

**L'ENCEPHALOGRAPHIE FRACTIONNÉE** (Fractional Encephalography). Giovanni Ruggiero. 510 pp. Illust. Masson et Cie, Paris, 1957. Fr. fr. 13.500.

Cet ouvrage très bien illustré de documents personnels constitue, sauf erreur, une des premières études l'envergure du système nerveux central parues dans la littérature radiologique française. L'auteur nous fait part de son expérience neuroradiologique depuis son association avec le Professeur Marcel David.

L'encéphalographie fractionnée consiste en une encéphalographie faite avec une petite quantité d'air et peut se pratiquer même dans les cas d'hypertension intra-crânienne, à condition de ne pas soutirer de grandes quantités de liquide céphalo-rachidien. Cette méthode présente l'avantage sur l'encéphalographie totale de ne pas être douloureuse et donc de ne pas nécessiter d'anesthésie mais, par contre, elle présente l'inconvénient d'avoir à multiplier les clichés et les incidences pour obtenir une étude détaillée et complète de tout le système ventriculaire et des espaces sous-arachnoïdiens.

Ruggiero a certainement eu un bon maître en Lindgren et son livre a une grande valeur pour tout neuroradiologue, car l'encéphalographie fractionnée, à mon avis, a su mettre l'accent sur l'étude des citermes et des sillons sous-arachnoïdiens qui ne présentent plus de secret pour ces deux auteurs. Le lecteur goûtera surtout la première moitié de l'ouvrage qui traite de la technique de l'examen et de l'étude fine de l'espace sous-arachnoïdien. Les lésions de la fosse postérieure sont également étudiées dans un chapitre excellent. L'étude des lésions expansives supra-tentorielles est très intéressante mais elle n'apporte pas d'autre contribution à la littérature neuroradiologique que de nous présenter l'expérience de l'auteur dans les différentes lésions qu'il a rencontrées et l'on ne peut pas dire que son expérience diffère beaucoup de celle des autres, même de ceux qui emploient encore la ventriculographie, l'angiographie ou l'encéphalographie totale et qui peuvent prétendre faire une très belle étude de l'espace sous-arachnoïdien par cette dernière méthode tout en limitant les incidences nécessaires.

**PERINATAL LOSS IN MODERN OBSTETRICS.** Robert E. L. Nesbitt, Jr., Albany Medical College, Union University, Albany, New York. 432 pp. Illust. F. A. Davis Company, Philadelphia; The Ryerson Press, Toronto, 1957. \$13.75.

This is an obstetrician's book on preventive obstetrics. The great emphasis is on the other patient, the fetus-in-utero. In the forefront are the three main hazards—prematurity, anoxia and trauma. Not only is the immediate loss considered but also the remote outlook is emphasized—the continuum of the living, cerebral palsy, epilepsy, mental defect, and other defects in the living. In about a third of cases, no pertinent knowledge can be brought to bear on the problem; in many others only the method of dying is known.

This is a dynamic approach through the available information, statistical, immunological, genetic, clinical, as well as the morbid anatomical. The detail is pertinent, and the illustrations are clear.

Dr. Nesbitt is professor of obstetrics at Albany Medical College, and one of the continent's foremost writers; the subject matter is a source of heartache to over half a million Americans and a proportionate number of Canadians annually.

This book deserves a wide audience.

**CHRONIC SCHIZOPHRENIA.** Thomas Freeman, University of Glasgow, John L. Cameron, Chestnut Lodge Sanitarium, Rockville, and Andrew McGhie, University of Glasgow. 158 pp. International Universities Press, Inc., New York, 1958, \$4.00.

This monograph is called by its authors a "clinical, interpretative and therapeutic study of chronic schizophrenia." Based on research at the Glasgow Royal

Mental Hospital, it deals with patients severely disintegrated or dominated by long-standing fixed paranoid delusions. The central theme in this research was the therapeutic utilization of the "interpersonal forces that promote or impede recovery".

This volume, however, gives much more than a research report. It presents the reader with a concise and lucid account of the psychoanalytic concept of the mind, followed by a similarly well-written review of psychoanalytic theories of the psychopathology of schizophrenia from Freud (1896) to Katan (1954). The disturbance of various functions (e.g. perception, thinking, memory) is then presented and discussed in separate chapters, illustrated with the authors' own case material. An inability to differentiate the self from the environment is offered as a "basic disturbance" from which all other schizophrenic manifestations can be elaborated. Although the research was psychoanalytically oriented, the authors' outlook was broad, enabling them to blend successfully psychoanalysis with Kraepelinian nosology, as well as with dynamic interpersonal theories of Bleuler, Meyer and Sullivan respectively.

The last section of this monograph gives a detailed and very practical account of the authors' methods used in the treatment and rehabilitation of chronic hospitalized schizophrenic patients. By attention to every detail in staff-patient relationship and in everyday nursing care, a therapeutic atmosphere is created which promotes in the patients the re-establishment of contact with their environment, and with reality. The technique presented would transform a stagnant chronic ward into an active treatment situation.

This book is particularly recommended for every physician or nurse in charge of a ward with chronic schizophrenic patients, as an excellent and practical guide for treatment. It is also recommended for the student in psychiatry who wishes to obtain a clear and succinct account of analytical theories of schizophrenia.

**TUMORS OF THE SOFT SOMATIC TISSUES: A Clinical Treatise.** George T. Pack, Memorial Center for Cancer and Allied Diseases, and Irving M. Ariel, New York Medical College, New York. 820 pp. Illust. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York, 1958. \$30.00.

Any book such as this, which describes the experiences of two able surgeons in handling tumours of soft parts for a period of 25 years, deserves considerable attention. Collaborating with Drs. Pack and Ariel in writing this book are a number of other authorities familiar with the problem of soft tissue tumours.

One of the more fascinating chapters is the section on classification and natural history of tumours of soft somatic tissues. This includes definitions and classifications; the question of hereditary and congenital effects; the role of trauma in inducing sarcomas; a discussion on whether benign somatic tumours become malignant, and whether tumours of soft somatic tissues metastasize to regional lymph nodes. The experience of the authors on all these points is very well described.

The sections on the general principles of therapy applied to these tumours, and their application to specific tumours, are of great practical interest.

The chapter on sarcomas of the soft somatic tissues in infants and children is helpful, since rather little

has been written about these tumours in children and infants. The last section of the book, on prognosis, shows the end results of the treatment of sarcomas of the soft somatic tissues, summarizes the work of all these men, and encompasses a wide experience.

The book is well bound. The illustrations, for the most part, are superb and the type is readily legible. Whether one agrees or not with all of the ideas expressed in this book is of no major consequence, since the book itself has much in it of extreme value to all of us, whether pathologists or surgeons, faced with the problems of handling tumours of the soft somatic tissues.

**ERYTHROBLASTOSIS FETALIS: Including Exchange Transfusion Technic.** F. H. Allen, Jr., and L. K. Diamond, Harvard Medical School, Boston. 143 pp. Little, Brown and Company, Boston and Toronto, 1957. \$4.00.

This book cannot be too highly praised. The authors, well known and outstanding in this field, need no introduction. The book itself has drawn the highest commendation from such eminent authorities as Dr. Nicholson Eastman and Dr. Edith Potter. Its outstanding quality is the simple handling of a complex subject. If the gift of the maestro be to make a difficult subject simple, this book is eloquent testimony of this truth. The problems associated with Rhesus incompatibility are treated not singly, but more correctly fitted into the general pattern of blood group specificity. If this monster jig-saw, involving as it does 49 key factors, presents a frightening prospect, the authors are reassuring in their emphasis on those things happening most commonly—in this respect it is well to take note of the frequency of erythroblastosis foetalis due to ABO incompatibility, occurring as it does twice as often as that due to Rhesus incompatibility though usually of less severe degree. Prophylaxis, treatment of the newborn, including a full account of the technique of exchange transfusion, and prognosis are alike handled with great clarity. With respect to prognosis, the relationship of Rhesus incompatibility to ABO grouping of mother and fetus is discussed in some detail. The relative advantage of ABO incompatibility under these circumstances in obviating Rhesus sensitization is pointed out. At a time when the position of blood transfusion is being reassessed, the remarks of these authors have special weight. The supreme importance of accurate Rhesus typing preparatory to blood transfusion is obvious enough—the statement that the multiplicity of blood factors makes the chance of a completely compatible blood transfusion rather less than 10% is barely modified by the succeeding statement that the danger of sensitization and subsequent production of erythroblastosis foetalis is very small; and emphasizes Dr. Bruce Chown's fears on the perils attached to the increasing use of blood in hospitals across the country today.

**UROLOGIC INJURIES IN GYNECOLOGY.** Henry C. Falk. 265 pp. Illust. F. A. Davis Company, Philadelphia, Pa.; The Ryerson Press, Toronto, 1957. \$8.25.

"Urinary incontinence in women, the main subject of this monograph, is one of the most frightful afflictions of human kind. Hour by hour and night and day, a leakage wets, excoriates and hurts the victim. Clothes are ruined, the bed . . . a nightmare . . .

(Continued on page 520)

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(Continued from page 518)

a pariah is made. Dr. Falk has exposed the fate of the sufferer with the zeal of a Marion Sims. His literary style and diagrams are vigorous and clean cut." This quotation comes from the foreword by Professor Edwin M. Robertson of Queen's University, Kingston.

One hundred illustrations and 248 pages of large type encompass the whole field of diagnosis, management and treatment in a surprisingly brief fashion. This is a brilliant monograph directed to a restricted audience.

**ENDOCRINE ASPECTS OF BREAST CANCER.** Edited by Alistair R. Currie. 339 pp. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1958. \$6.35.

This text consists of papers delivered at a conference held at the University of Glasgow, July 8-10, 1957. The participants in the conference are a distinguished group of clinicians and investigators widely recognized for their interest in and contributions to the field of breast carcinoma.

The proceedings are divided into four parts—clinical studies, pathology, hormone studies, and experimental pathology. Each of the four sections is followed by a discussion and summary, and the text is completed by a review of the conference by Professor Illingworth. The latter is a very neat epitome of all that transpired.

Part one, the clinical section, deals with the effect on carcinoma of the breast of adrenalectomy, radiation hypophysectomy and surgical hypophysectomy, a comparison of the results of the various procedures, and physiological and metabolic effects of these procedures.

Part two, the section on pathology, is short. It deals with pharyngeal hypophysis, histological and chemical studies on adrenal glands taken from patients with breast carcinoma, and histohormonal studies on the human anterior pituitary. There is also a section on a post-mortem survey on adult breasts, with observations on gonad and pituitary. There is included a paper on the microanatomical changes of the breast as a result of hormonal stimulation.

Part three, hormone studies, is chiefly of interest to the biochemist. However, the papers on anterior pituitary mammotrophins are of interest to the clinician, as they relate to attempts to predict satisfactory responses of metastatic breast carcinoma to adrenalectomy and hypophysectomy. The section is admirably summed up by G. F. Marrian.

The fourth section deals with experimental pathology, and will be of interest to those occupied in the study of breast tumours in laboratory animals.

This book is particularly timely, with all the current discussion and debate concerning the etiology of carcinoma of the breast, and the palliation of carcinoma of the breast by hormonal methods. Those interested in this subject will find stimulating reading here. It is profuse with theories and facts. Even if one is not interested in the minutiae of investigative technique and analysis, the discussion and summary at the end of each section and the final summary will bring one up to date on this new and intriguing field of study.

**ABNORMAL LABOR.** L. A. Calkins, Kansas City. 70 pp. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1958. \$3.00.

Dr. Calkins' publication, "Abnormal Labor", is a brief and useful guide for all practitioners who wish a reliable source of information relating to the practice of obstetrics. It must be pointed out, however, that the author's statement that fetal mortality in immature breech presentations is double that of immature cephalic presentations has not been the reviewer's experience, nor has the reviewer found Cæsarean section as effectual a procedure as the author in these cases. "Trial forceps" is a procedure never to be reticent about as long as the obstetrician resorts to Cæsarean section the moment that he realizes that vaginal delivery is not a safe procedure.

It might be indicated that measuring the number of uterine contractions is a more reliable means of measuring the length of the second stage than any other.

The book is original, unique and a valuable addition to any library.

**THE MEDICAL MANAGEMENT OF CANCER.** H. D. Diamond, Cornell University, New York. 179 pp. Illust. Grune & Stratton, Inc., New York, 1958. \$6.75.

The increasing number of malignant tumours that are being treated by chemotherapeutic or ionizing radiation measures (with or without surgery) makes it essential for the practising physician to become better acquainted with these definitive methods of treatment. This monograph is therefore very timely.

This is a small but very compact book, and has a wealth of material in it. The book is divided into two sections: (1) management of the cancers that are primarily treated by medical means, e.g., malignant leukæmias and plasma cell myelomas; (2) medical management of cancers, in which the primary treatment is surgical, such as the neuroblastomas and cancers of the lung, thyroid, ovary, breast and prostate. The last chapter deals with the use of intracavitary injection of radioisotopes such as radioactive gold, phosphorus and yttrium.

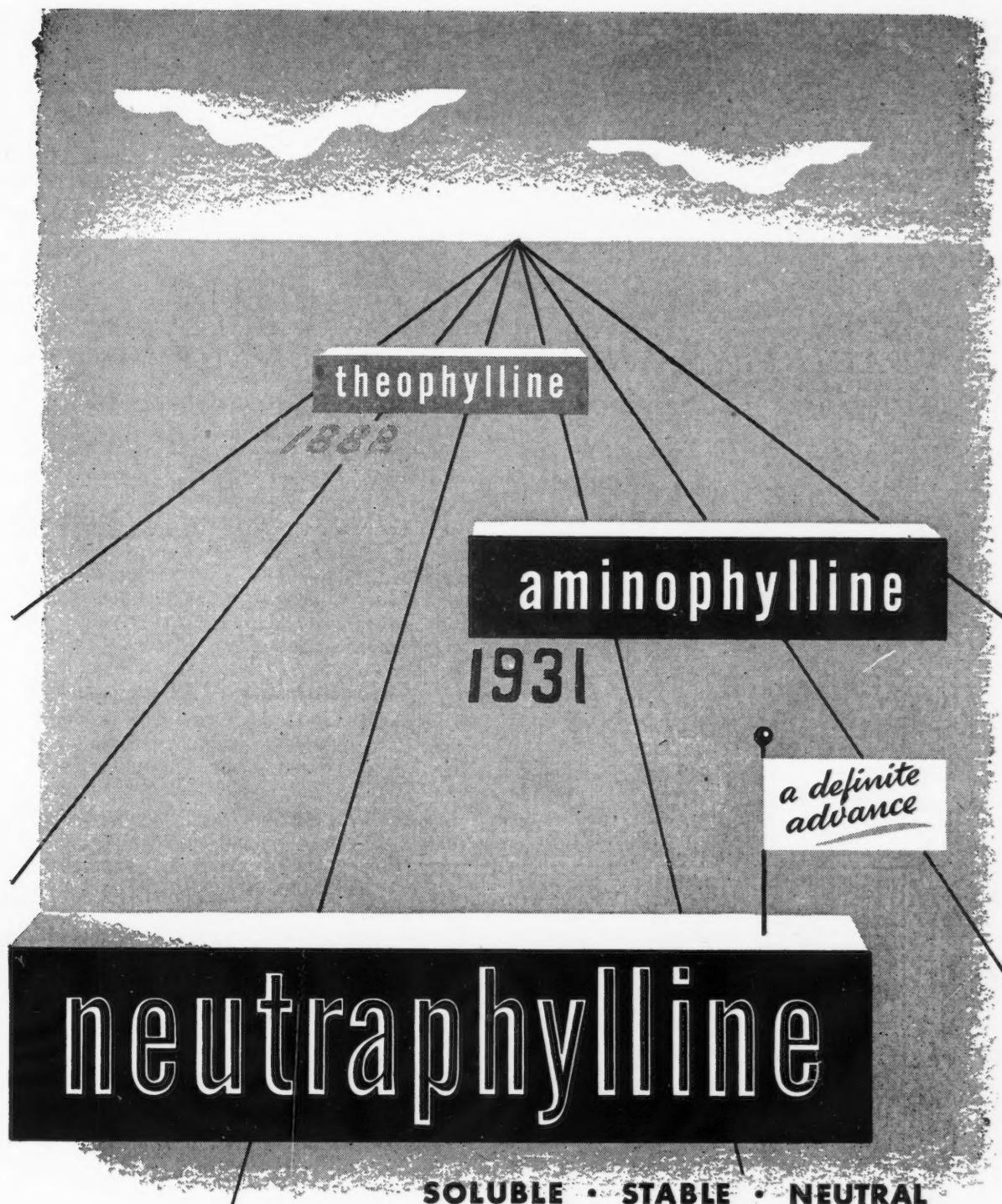
Each subject is dealt with in a lucid, up-to-date fashion, with the emphasis on definitive treatment. One cannot help but feel that the author has written this monograph from an extensive personal experience.

The paper and printing are excellent, and there are many good illustrations. Some readers may be annoyed by the small print in limited parts of the book. This monograph is highly recommended to all interested physicians.

**PERIPHERAL VASCULAR DISEASE.** A. J. Barnett, Assistant Director, and J. R. E. Fraser, Sometime Registrar, Alfred Hospital Clinical Research Unit, Melbourne, Australia. 219 pp. Illust. Melbourne University Press; The Macmillan Company of Canada Limited, Toronto, 1958. \$9.75.

This monograph on vascular diseases of the extremities is a particularly useful one for the busy practitioner. In brief but adequate descriptions it contains most of the information needed in clinical diagnosis. Particularly useful are the chapters on physiology and on diagnostic methods. The illustrations are numerous and well chosen. This volume can be recommended to both the general physician and the internist.

(Continued on page 523)



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(Continued from page 520)

**SKIN GRAFTING.** J. B. Brown and F. McDowell. 411 pp. Illust. 3rd ed. J. B. Lippincott Company, Philadelphia and Montreal, 1958. \$15.00.

This is the third edition of a book which in its first edition appeared under the title "Skin Grafting of Burns". Much of this volume is taken up with the treatment of burns, and with the types of skin replacement of value in any particular situation. Chapters on certain types of trauma and their treatment by skin transference have been added. A chapter on post-mortem skin homografts is included. Pedicle grafting is thoroughly discussed.

This book, written by two experts, well illustrated and well produced, will prove to be an extremely useful reference work for all who are called upon, either occasionally or routinely, to transplant skin.

**MEDICAL HISTORY OF THE SECOND WORLD WAR:**  
Army Medical Services — Campaigns, Vol. II. F. A. E. Crew. 537 pp. Illust. Her Majesty's Stationery Office, London, 1957. 84s.

This volume records the story of military medicine, and of the men who practised it, frequently under the most difficult circumstances and in some of the most critical phases of World War II. These included the defence and fall of Hong Kong; the campaign in Malaya and the fall of Singapore; the military occupation of Iceland and the Faroes; the final campaign in Libya from the battle of El Alamein to the passage of the Eighth Army into Tunisia; and the campaign in North-West Africa. It also includes sections which deal with the health of the troops of the Middle East Force 1942-43, and the forces' Army Psychiatric Service as well as its Pathology and Transfusion Service.

This is the story of the courage and fortitude of the members of the Army Medical Services and of those whom they served. The most outstanding parts of this narrative are the fall of Hong Kong and Singapore and the campaign in Malaya. Much of this is based on records by participants who, in spite of long years of captivity, of suffering and humiliation, maintained remarkable and objective chronicles of events in which they themselves were participants. In the campaigns in Libya and in North-West Africa, mechanization and the continuous introduction of new weapons created many new medical problems. These included marked increases in accidental injuries; there were all the varied lessons to be learned in the planning of combined large-scale assault landings; and the introduction of the aeroplane as an instrument of evacuation. The occupation of Iceland and the Faroes presented new medical problems of cold weather operation, whereas the Middle East operations differed markedly from all others, particularly in respect to the physico-climatic features. For this reason, a comprehensive review of the health of the Middle East Command is included. Furthermore, it was in this Command that the earliest phases in the rapid development and acceptance of military psychiatry occurred. The accounts of this and of the Army Pathology and Transfusion Service in the Middle East merit special attention.

Among its many attributes, this volume emphasizes that the Army Medical Services learned quickly the medical lessons of war and applied them just as promptly to the benefit of the Armed Forces.

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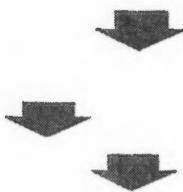
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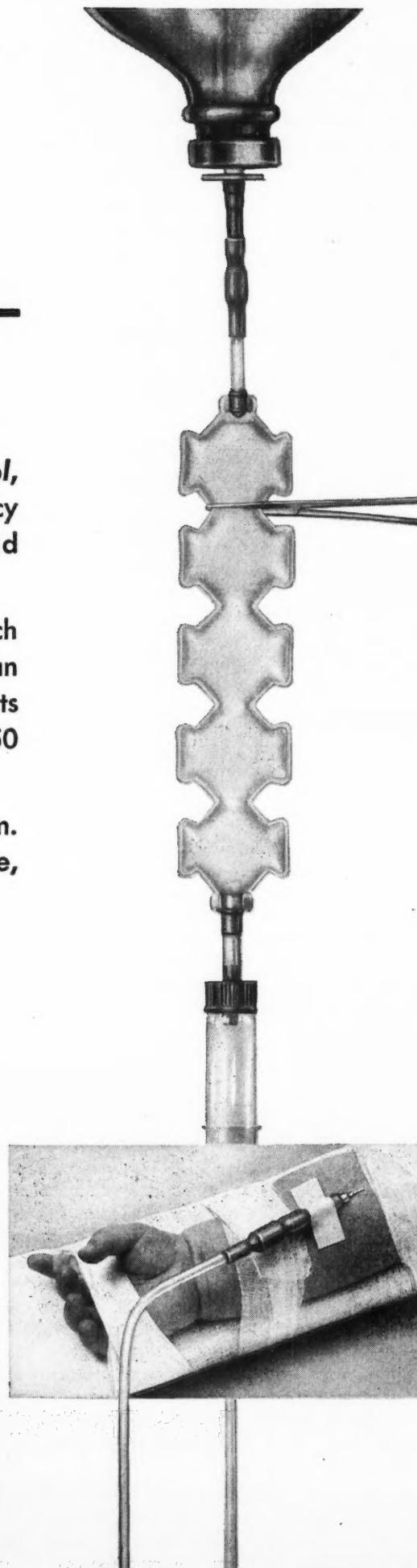
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## Books Received

Books are acknowledged as received, but in some cases reviews will also be made in later issues.

**The Yearbook of Modern Nursing 1957-58.** A Source Book of Nursing. Edited by M. Cordelia Cowan. 460 pp. G. P. Putnam's Sons, New York; McAlpin & Co., Limited, Toronto, 1958.

**Classification of Atherosclerotic Lesions.** Report of a Study Group. WHO Technical Report Series No. 143. 20 pp. World Health Organization, Palais des Nations, Geneva, 1958. \$0.30.

**Expert Committee on Biological Standardization.** 11th Report. WHO Technical Report Series No. 147. 38 pp. World Health Organization, Palais des Nations, Geneva, 1958. \$0.30.

**Regional Ileitis.** B. B. Crohn and H. Yarnis, New York. 239 pp. Illust. 2nd ed., revised. Grune & Stratton, New York and London, 1958. \$7.25.

**Milestones in Modern Surgery.** Edited by A. Hurwitz and G. A. Degenshein, New York. 530 pp. Illust. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York, 1958. \$15.00.

**Chirurgie infantile d'urgence (Emergency Surgery in Childhood).** M. Fèvre, Paris. 2nd ed. Completely revised. 718 pp. Illust. Masson & Cie, Paris, 1958. 8.000 fr.

**Chirurgie d'exérèse dans la tuberculose pulmonaire: technique, indications, résultats (Resection Surgery in Pulmonary Tuberculosis: Technique, Indications, Results).** D. Honoré, Liège. 216 pp. Illust. Masson et Cie, Paris; Georges Thone, Liège, 1958. 3.300 fr.

**Les sinusites de l'enfance (Sinusitis in Childhood).** J. Terracol & Y. Guerrier. 166 pp. Illust. Masson & Cie, Paris, 1958. 1.400 fr.

**Amélioration et reproduction des radiographies par modulation électronique: le logetron (Improvement and Reproduction of Radiograms by Electronic Modulation: the Logetron).** A. Jutras and H. Fischgold. 122 pp. Illust. Masson et Cie, Paris, 1958. 4.500 fr.

**List of Films on Human Anatomy and Embryology.** 213 pp. 2nd ed. Published by Netherlands Scientific Film Association, Utrecht, and International Scientific Film Association, Paris, 1957.

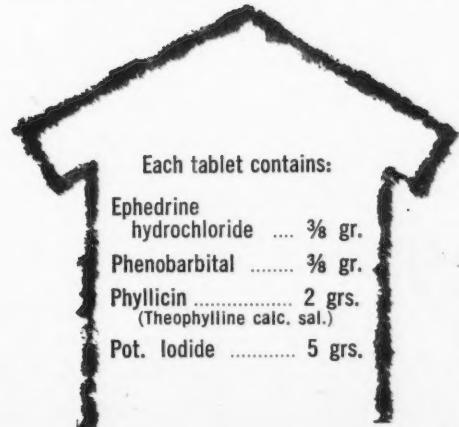
**Roentgenanatomie der Neugeborenen—und Säuglingslunge (Radiologic Anatomy of the Lung of New-Born Babies and Infants).** Z. Zsébök, Budapest. 160 pp. Illust. Georg Thieme Verlag, Stuttgart; Intercontinental Medical Book Corporation, New York, 1958. \$17.85.



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PICKWICK, S., *Textbook of Medicine*, Jones and Jones, London, 1st ed., p. 30, 1955.

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(Continued on page 40)

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**MEDICAL NEWS in brief**

(Continued from page 494)

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MEMORIAL FELLOWSHIPS**

Applicants for these Fellowships shall be graduates in medicine of an approved Faculty of Medicine and (a) shall have had, after receipt of their degree, not less than three years of post-graduate study of which at least two shall have been in a field related to the diagnosis and/or treatment of cancer; (b) shall under this Fellowship pursue a program

of two years' further post-graduate study of the diagnosis and/or treatment of cancer acceptable to the Advisory Committee on Fellowships of the Canadian Cancer Society; and (c) shall express a firm interest and assume the moral obligation to practise his/her profession subsequently in Canada with a particular interest in cancer.

One Fellowship will be awarded annually. A Fellowship is tenable for two years and has a value of \$4000 per annum for single Fellows and \$4500 per annum for married Fellows.\*

Application forms may be obtained from the Canadian Cancer Society, 800 Bay St., Toronto 5, Ont. Applications should be submitted not later than October 1, 1958.

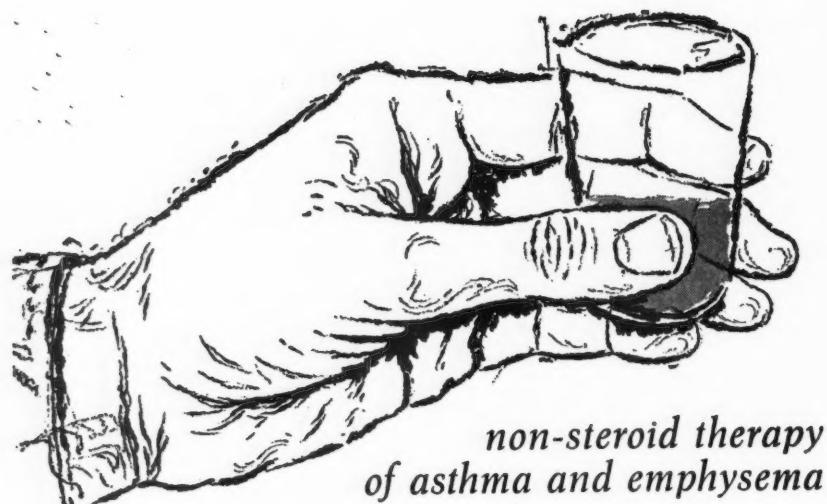
**BRITISH EMPIRE CANCER  
CAMPAIGN EXCHANGE  
FELLOWSHIPS**

The British Empire Cancer Campaign has established two Fellowships per annum for Canadians.

These Fellowships are tenable for twelve months and of an approximate value of £1500 per annum. Travelling expenses of the Fellows from their Canadian residence to England and return will be borne by the National Cancer Institute of Canada. If necessary, an allowance will also be paid for expenses in connection with the work undertaken. The Fellowships are open to those engaged in the clinical and allied sciences and to those working in fundamental research related to cancer.

Application forms may be obtained from: The National Cancer Institute of Canada, 800 Bay Street, Toronto 5, Ont.

Applications should be submitted to the above address not later than November 1, 1958. Awards will be announced December 15, 1958. Fellowships will become tenable July 1, 1959.

**oral ELIXOPHYLLIN**

Just as with I.V. aminophylline,\* high theophylline blood levels reached in minutes — from a single dose.\*



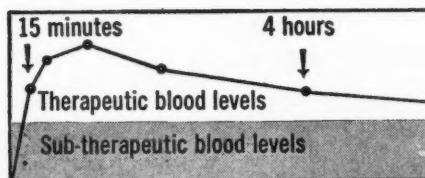
After absorption, theophylline is slowly eliminated. Therapeutic blood levels endure for hours.\*



This predictability of blood levels permits quite constant therapeutic blood levels night and day, providing relief of wheezing, dyspnea, cough, and protection against acute attacks for most patients.\*

**DOSAGE: First two days:**

- 45 cc. (three tbsp.) on arising;
- 45 cc. (three tbsp.) on retiring;
- 45 cc. (three tbsp.) once midway between above doses (about 3 P.M.)



After two days of therapy the size of doses should be slightly decreased. Each tablespoonful contains: theophylline 80 mg., alcohol 3 cc. Prescription only — bottles of 16 fl. oz.

*Sherman Laboratories*  
Windsor, Ontario

\*Reprints of these studies on request.

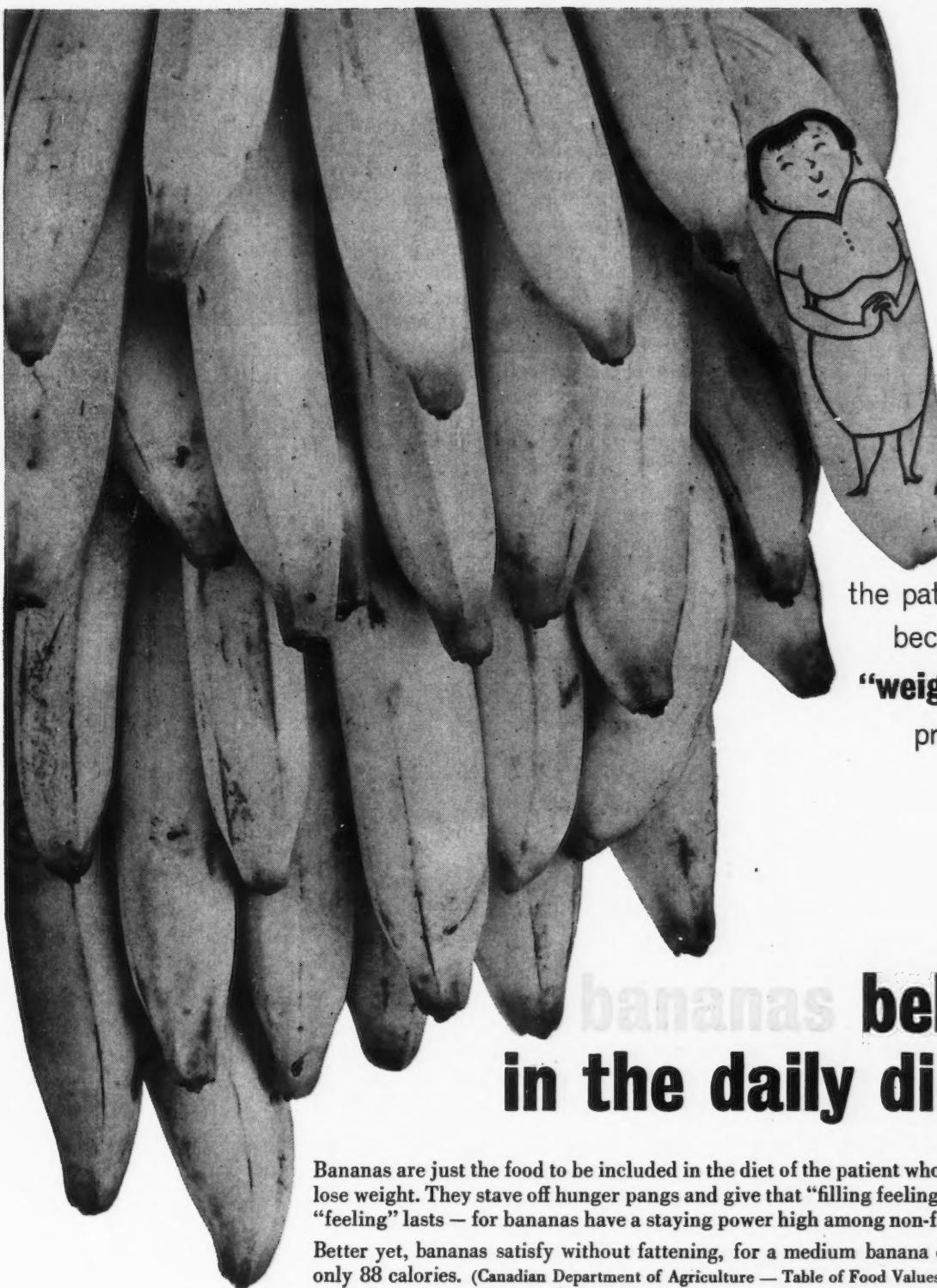
**NATIONAL IMMUNIZATION  
WEEK**

National Immunization Week, organized by the Health League of Canada in co-operation with the official health departments, will be observed the week of September 22 for the 16th consecutive year. The Week is an annual reminder to parents that immunization will protect their children from certain communicable diseases.

**EXPERIMENT IN  
EDUCATION**

Great Britain has long been a stronghold of conservatism in medical education, perhaps because the all-powerful General Medical Council has laid down such detailed recommendations for a curriculum. However, the Council in 1957 modified its stand, in order to give greater liberty to

(Continued on page 52)



## bananas belong in the daily diet

Bananas are just the food to be included in the diet of the patient who needs to lose weight. They stave off hunger pangs and give that "filling feeling." And the "feeling" lasts — for bananas have a staying power high among non-fatty foods.

Better yet, bananas satisfy without fattening, for a medium banana contains only 88 calories. (Canadian Department of Agriculture — Table of Food Values.)

Bananas are also rich in taste appeal and per calorie contain more than their quota of most of the vitamins lacking in many weight-reducing diets.

### high in appetite satisfaction — bananas fill without fattening

Help your patient to EASIER WEIGHT CONTROL — only 88 calories in a medium banana . . . and they satisfy!

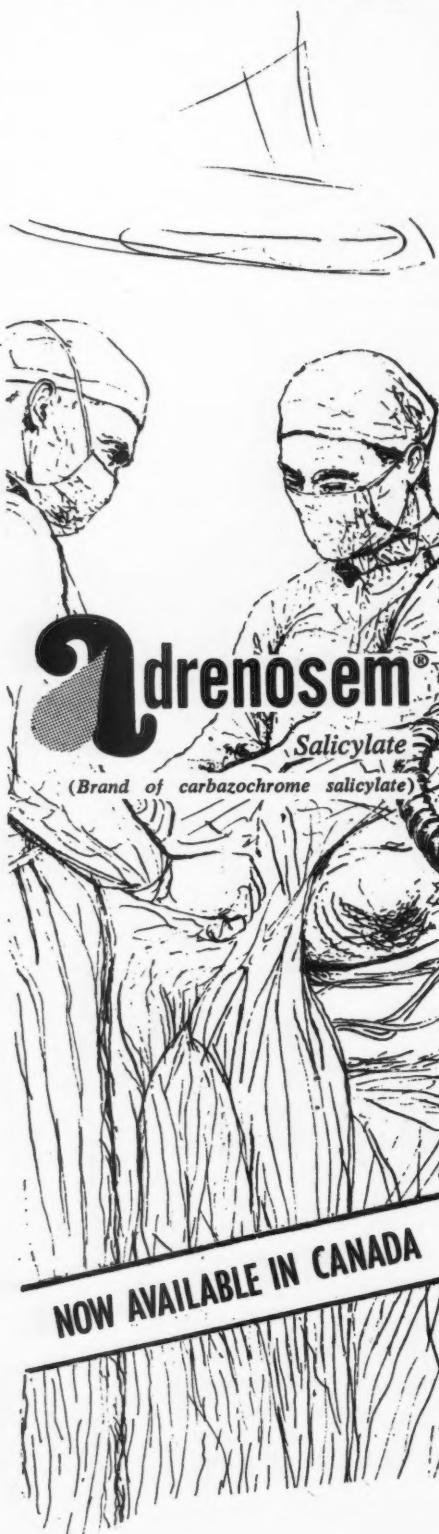
Help your patient to GREATER VITALITY — Vitamins A, B<sub>1</sub>, B<sub>2</sub>, C, and niacin in every banana.

Help your patient to BETTER DIGESTION — smooth, bland, bananas contain helpful pectins and non-irritant fibers.

And why not HELP YOURSELF TO A BANANA — they taste so good.

CANADIAN BANANA COMPANY LTD.

## to control bleeding



The S. E. MASSENGILL Company  
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### MEDICAL NEWS *in brief*

(Continued from page 50)

medical schools devising an experimental curriculum.

A further step in modifying the British curriculum has recently been taken with the formation of an Association for the Study of Medical Education which is designed to represent all those interested in medical education. The Association will exchange information, organize meetings, maintain an information bureau, encourage and conduct research into matters connected with medical education, and hold its first conference on September 25 and 26. The subject of the conference will be "Experiment in Education". The Executive Committee for the new Association consists of a number of eminent British educators, including the Presidents of the Royal Colleges.

### TRENDS IN SOVIET PSYCHIATRY

Lesse (*Am. J. Psychiatry*, 114: 1018, 1958) has summarized clinical and research trends in Soviet psychiatry after a visit in which he was able to discuss the subject with psychiatrists in leading Soviet centres. He notes that clinical neurology and psychiatry are closely integrated there, and that the general dispensaries in a Russian city have a psychiatric section. If a patient needs more complicated treatment, he is referred to a special dispensary for adults or children or to a "station" serving as an intermediate between the dispensary and the mental hospital. The station may take patients in for from one day to one month, or give them treatment during the day, returning them to their homes at night. Admission to mental hospital is said to be voluntary except in the case of criminals.

Lesse stresses the large numbers of medical personnel available in hospitals, and the use of personnel to supervise mental patients in their homes. Psychotherapy in the Soviet Union bears little resemblance to techniques commonly practised in the West. For example, psychoanalysis is not used at all, but the patient is treated with emphasis on his relation to his environment, i.e. he is treated

(Continued on page 58)

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Inflammation and edema associated with: trauma and infection • cellulitis • abscess • hematoma • thrombophlebitis • sinusitis • uveitis • chronic bronchitis • leg ulcer • chronic bronchiectasis.

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**Administration:** VARIDASE Buccal Tablets should be retained in the buccal pouch until dissolved. For maximum absorption patient should delay swallowing saliva.

**Dosage:** One tablet four times daily for a minimum of three days. When infection is present, VARIDASE Buccal Tablets should be given in conjunction with an antibiotic such as ACHROMYCIN\* V Tetracycline and Citric Acid.

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## Chronic Bronchitis

Loosens cough...resolves  
inflammation...  
Increases antibiotic  
penetration.<sup>1</sup>

## Thrombo- Phlebitis

Relieves thrombotic  
process, controls  
swelling...gives  
dramatic  
relief of pain.<sup>1,2</sup>

## Skin Infections

Furuncles,  
carbuncles,  
abscesses...checks  
swelling and  
pain...hastens healing.<sup>1,2</sup>

# Watch it work in your practice!

MEDICAL NEWS *in brief*

(Continued from page 52)

on the lines that he will derive great benefits and security only from the collective strength of his group. Sleep therapy is widely used, because of Pavlov's teaching of protective inhibition. This is achieved by giving sufficient Sodium Amytal to keep the patient asleep 16 to 18 hours daily through 10 to 15 days. Insulin coma is extensively used, but ECT is rare. Psychosurgical procedures were banned in 1950. Chlorpromazine (known in the USSR as Amazine)

and rauwolfia are widely used, as is amphetamine. Hypnosis is rare. Inhalation of 80% nitrous oxide and 20% oxygen is used in some cases of schizophrenia or depression.

#### BRITISH MEDICAL ASSOCIATION: APPOINTMENT OF SECRETARY

At a meeting of Council at B.M.A. House on May 7, the British Medical Association appointed Dr. Derek P. Stevenson as

secretary of the Association with effect from November 12, 1958. Dr. Stevenson has been on the staff of the B.M.A. since 1946 and was appointed deputy secretary in 1948. He succeeds Dr. Angus Macrae, who made so many friends in Toronto when he visited us in 1955.

At the same meeting, Dr. Ian D. Grant and Dr. J. A. L. Vaughan-Jones were elected vice-presidents of the British Medical Association in recognition of their distinguished services. Members of the College of General Practice of Canada will recall with pleasure Dr. Grant's visit to their annual scientific meeting last year in Montreal.



## DYSAMENE\*

*Relief from menstrual distress*

One therapy for the entire cycle of menstrual distress.

#### INDICATIONS—

- Primary dysmenorrhea.
- Primary dysmenorrhea associated with premenstrual tension.
- Premenstrual tension.

\* Reg. T.M. Austin Laboratories Limited



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#### TRIAMCINOLONE (ARIS- TOCORT), A NEW CORTI- COSTEROID HORMONE IN THERAPY OF ALLERGY

The effects of triamcinolone (Aristocort) were studied by Feinberg *et al.* of Chicago on 70 patients with allergic or suspected allergic manifestations; 52 had asthma, 5 had hay fever and 12 perennial vasomotor rhinitis. Virtually all of the patients received the same relief as they did with other anti-inflammatory hormones. The initial 24-hour dose varied from 8 to 16 mg., and the average maintenance dose was 6 mg. The side effects were similar to those of other hormones, except for the marked diuretic effect of triamcinolone. Loss of weight was also common though not universal. In two non-obese patients the weight loss was 20 lb. in several weeks. A peculiar syndrome of headache, sleepiness, dizziness and weakness occurred in a few patients, and some preferred their allergies to this prostrating effect of the drug. It was not relieved by addition of supplementary sodium or potassium tried in 3 cases. The drug does not stimulate the appetite and may even depress it.—J. A. M. A., 167: 58, 1958.

#### THE PANCREAS: CONTRIBU- TIONS OF CLINICAL INTEREST

Johnson and Kalser (*Gastroenterology*, 34: 543, 1958) review 126 papers dealing with physi-  
(Continued on page 62)

Evidence continues to accumulate verifying the effectiveness of Gelatine in the treatment of brittle fingernails. Investigators report that the nails show objective evidence of improvement.<sup>1,2,3,4</sup> Furthermore, patients often volunteer that their nails "feel stronger," "look smoother," and "I can pick up things without them hurting."<sup>1</sup> Evidently the subjective sensations associated with improvement are nearly as important to some patients as the positive physical change in the nails' appearance.

### Improvement Noted in 81% of Patients

See the chart below for a summary of the effect of Knox Gelatine in brittle fingernails as observed in all published reports. Photographic evidence of improvement, much of it in color taken before and during treatment, is available for most of the patients.<sup>1,2,3</sup> Please note, however, that where Gelatine was used in the treatment of pathological conditions associated with brittle fingernails only in psoriasis did the data show definite improvement.<sup>1,3,4</sup>

### Response to Gelatine in Brittle Fingernails

References	Dosage	Duration of treatment	No. patients w/ brittle nails	No. patients improved	No. patients w/ brittle nails and other pathology	No. patients improved
1. Rosenberg, S., Oster, K. A., Kallos, A. and Burroughs, W.: <i>A.M.A. Arch. Dermat.</i> 76:330, (September) 1957	7 Gm./day	3 months	50	43 (86%)	32 <sup>a</sup>	9
2. Schwimmer, M. and Mulinos, M.G.: <i>Antibiot. Med. &amp; Clin. Therapy</i> 4:403, (July) 1957	7.5 Gm./day	11-16 weeks	18	15 (83%)		
3. Rosenberg, S. and Oster, K. A.: <i>Conn. State Med. J.</i> 19:171, (March) 1955	7 to 21 Gm./day	15 weeks	36	26 <sup>b</sup> (72%)		
4. Tyson, T. L.: <i>J. Invest. Dermat.</i> 14:323, (May) 1950	7 Gm./day	13 weeks	12	10 <sup>c</sup> (83%)		
<b>Totals</b>	<b>7-21 Gm.</b>	<b>11-16 weeks</b>	<b>116</b>	<b>94 (81%)</b>	<b>32</b>	<b>9 (28%)</b>

- a. Gelatine improved psoriatic nails in 5 out of 12 cases. In onychomycosis and other pathological conditions of the nail it was of no appreciable help.
- b. Of the failures, 2 had congenital disease of the nails, 3 were diabetics and 3 took the medication for less than one month.
- c. One patient with psoriasis and arthritis and one patient with psoriasisform nail changes showed improvement in 2 and 3 months respectively.

# BRITTLE FINGERNAILS

### Important Note

The pharmacodynamic effects of Gelatine are manifested through its high Specific Dynamic Action, and therefore, depend upon adequate and prolonged intake. All published clinical research has been conducted using 7 to 21 grams (1-3 envelopes) of Knox Gelatine per day for the three to four months that are required for complete regrowth of the nails. Smaller dosage would induce a lesser specific dynamic action and thus prove ineffectual in correcting the brittle nail defects. More detailed information on brittle fingernails and reprints of the two more recent clinical reports are available on request. Please use the attached coupon.

Knox Gelatine (Canada) Limited  
Professional Service Department CA-4,  
140 St. Paul St. West, Montreal, Quebec

Please send reprints of the following articles:

- Rosenberg, S., Oster, K. A., Kallos, A. and Burroughs, W.: *A.M.A. Arch. Dermat.* 76:330, (Sept.) 1957.
- Schwimmer, M. and Mulinos, M.G.: *Antibiot. Med. & Clin. Therapy* 4:403, (July) 1957.

YOUR NAME AND ADDRESS

**MEDICAL NEWS in brief**

(Continued from page 58)

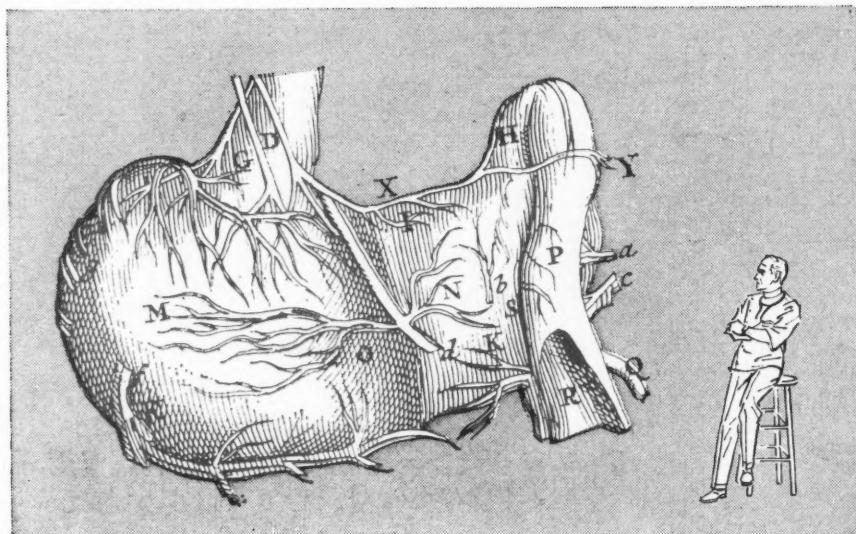
ology, experimental work and diseases of the pancreas, which appeared in 1956. Pancreatitis, both acute and chronic, is represented by some 45 papers. Conservative management and epidural block to the level of the fourth thoracic vertebra to relieve the severe pain of acute pancreatitis has been recommended by Lee. After recovery, gall-bladder studies should be undertaken and if a non-functioning gall bladder or stones are found they should be removed.

As regards chronic pancreatitis, attention is drawn to a report on the effects on pancreatic function of thoracolumbar sympathectomy and splanchnicectomy. Although the operation did not always limit the progression of the disease, patients treated in this fashion were clinically well and free of pain. Sphincterotomy in the hands of Doubilet and Mulholland produced 88% satisfactory relief of symptoms but had an immediate postoperative mortality of 5.3%. On the other hand, other authors found it disappointing.

Cystic fibrosis of the pancreas received a great deal of attention, and one writer reported 397 cases of this disease. It is interesting to note that of these patients 173 were dead at the time of the report, 90% of deaths resulting from chronic lung disease. Only 35 patients lived beyond the age of 10 years and the oldest died at 21. Several tests for detection of excessive chloride in the skin and for sweat collection were described and used successfully for screening suspected cases of fibrocystic disease of the pancreas.

An extensive review of the findings in carcinoma of the pancreas notes the difficulty of making an exact diagnosis. The ratio of carcinoma of the pancreas to all types of carcinoma in postmortem series is about 1.76 to 2.0%, with a sex ratio of 2-3 to 1 (male-female). Pain is the most frequent initial symptom and may be of three general types: (1) colicky pain in the upper right quadrant; (2) dull, steady midepigastric pain, radiating through to the back; and (3) paroxysmal pain beginning near the umbilicus and radiating widely to the back, chest and abdomen. Jaundice is the second and most significant symptom, the third most common being weight loss. Acute cholecystitis may be an initial indication of carcinoma in the pancreatic area; thrombo-phlebitis is common, emotional disturbances are common, and diabetes mellitus is present in some 10-13% of cases. The mass found in some 50% of cases is usually an enlarged gall-bladder. A number of papers deal with the treatment of carcinoma of the pancreas; the present poor results of surgery are attributed mainly to the inability of making an early diagnosis.

Ulcerogenic tumour, which has to be distinguished from beta-cell tumours of the pancreas, is reviewed in several papers. The relationship of these tumours to hypersecretion of glucagon and production of fulminating and often fatal peptic ulceration appears to be supported by some of the cases cited. One author suggests that in cases of refractory peptic ulcer a search should be made for pancreatic tumour, and its removal should be included in the surgical treatment of these ulcers. Other papers dealing with



**Q:** comprehensive medical treatment of peptic ulcer?

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Each 10 c.c. or tablet contains:

300 mg Dried Aluminum Hydroxide Gel  
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100 mg Methylcellulose

12.5 mg Adiphenine HCl

0.50 mg Benactyzine Hydrochloride

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► ANTACID: a balanced effective non-constipating combination.

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heterotopic and annular pancreas, pancreatic cysts and calcification, traumatic injuries to the pancreas, miscellaneous surgical aspects and physiology of the pancreas form the remainder of this review.

### PAN AMERICAN ATTACK ON LEPROSY

Early in July, a seminar on leprosy control was held in Brazil, at which a comprehensive leprosy control program for the whole American continent was discussed. It was estimated that the total number of cases of leprosy in the world is three to ten millions. The seminar evaluated the extent and scope of the leprosy problem in the Americas, reviewing mass treatment programs and methods of prevention and making recommendations for their organization and integration into the general public health services.

### THE MCGILL-MONTREAL GENERAL HOSPITAL RESEARCH INSTITUTE

The McGill-Montreal General Hospital Research Institute has marked the tenth anniversary of its foundation by the publication of a brochure describing some of the problems it is tackling. This Institute, which was the first of its kind to be established by a Canadian hospital, devotes practically all its energies to the solving of biochemical problems. Two-thirds of the Institute's work schedule is concerned with problems of the central nervous system, and with cancer. Members of the Institute are currently studying the effects on the central nervous system of such drugs as narcotics, anaesthetics, tranquillizers and alcohol. The Institute is also studying the biochemical behaviour of cancer cells, with special reference to the differences between them and normal cells. Since the problem of virus growth is related, investigations are being made on blood resistance to virus development. Other subjects under investigation include intestinal absorption, the biochemistry of the tubercle bacillus, and the biochemistry of immunity.

As is commonly the case, the McGill-Montreal General Hospital Research Institute is chronically short of funds and must find ade-

quate and regular financial support if it is to continue and develop its biochemical studies.

### A NEW URICOSURIC AGENT

An oral muscle-relaxing agent widely used during the past two years (zoxazolamine, commercially available as Flexin) has been found to have potent uricosuric properties. A preliminary report by Reed, Feichtmeir and Willett (*New*

*England J. Med.*, 258: 894, 1958) describes its effects in a patient with chronic traumatic arthritis and chronic gout. The drug was administered in a dose of 250 mg. three times a day and produced a remarkable drop in serum uric acid. One case of transient nephropathy reported in the past may have been caused by precipitation in the kidney of uric acid. The authors claim that the action of zoxazolamine resembles that of

(Continued on page 66)

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**"80% of epileptics... can, with appropriate care and encouragement, lead a normal life."**\*

\*Lord Cohen of Birkenhead: British M. J. 1:672, 1958.

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...an appropriate anti-epileptic for every clinical need

**for grand mal  
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Sodium (diphenylhydantoin sodium, Parke-Davis) is supplied in many forms—including Kapseals® of 0.03 Gm. and of 0.1 Gm. in bottles of 100 and 500

Kapseals (Dilantin 100 mg., phenobarbital 30 mg., desoxyephedrine hydrochloride 2.5 mg.), bottles of 100.

### Dilantin

### Phelantin

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### Milontin

**for the petit mal triad**

Kapseals (methsuximide, Parke-Davis), 0.3 Gm., bottles of 100.

Kapseals (phensuximide, Parke-Davis), 0.5 Gm., bottles of 100 and 1,000. Suspension, 250 mg. per 4-cc. teaspoon, 16-ounce bottles.

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Speed of absorption adds new emphasis to the benefits of true broad-spectrum action, minimum side effects and wide range effectiveness that have established ACHROMYCIN as an antibiotic of choice for decisive control of infection.

**REMEMBER THE V WHEN SPECIFYING ACHROMYCIN V.** New blue and yellow capsules (sodium-free)—250 mg. with 250 mg. citric acid, and 100 mg. with 100 mg. citric acid.

ACHROMYCIN V dosage; Recommended basic oral dosage is 6-7 mg. per lb. body weight per day. In acute, severe infections often encountered in infants and children, the dose should be 12 mg. per lb. body weight per day. Dosage in the average adult should be 1 Gm. divided into four 250 mg. doses.

## **ACHROMYCIN\* V CAPSULES**

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\*Reg. Trademark in Canada



**MEDICAL NEWS in brief**  
(Continued from page 63)

probencid. They recommend that any patient receiving the drug should maintain a good urinary output and that his urine should be alkalinized.

**CONTROL OF RADIATION HAZARDS**

The American College of Radiology has recently prepared an excellent practical manual on the medical and dental use of x-rays with control of radiation hazards.

This delightfully illustrated and succinctly written manual is designed for all who use x-rays in the healing arts. It first sets out the various radiation hazards and effects on the human body, together with sources of exposure and radiation dose and control. The second part of the brochure gives practical advice for limitation of radiation dosage and control in such procedures as chest fluoroscopy, dental radiography, abdominal and pelvic radiography, and examinations of limbs. This manual is easy to read and most attrac-

tively designed. It is recommended to all users of x-rays.

**GUIGOZ FELLOWSHIP FOR NUTRITION RESEARCH**

The 1959-1960 fellowship to promote nutritional research founded by the Guigoz Works will be awarded in the spring of 1959. Applicants are required to send to the International Children's Centre, Château de Longchamp, Bois de Boulogne, Paris XVI: (a) a curriculum vitae setting forth their work on biological and social problems concerning feeding or nutrition of infants and children; (b) a letter of introduction from one of their teachers; (c) a description of the studies which they wish to pursue with the help of the Guigoz fellowship.

The applicants should have a sufficient command of the French language.

At the end of the fellowship period, the fellow or fellows will be expected to send to the International Children's Centre a scientific study on the subject which they will have studied during the year.

The recipient of the 1958-1959 fellowship was Dr. Jean Chagnon, Aylmer East, Que.



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In all four Farmer's Wife Milks, vitamin D is increased to the highest permissible standard. All are vacuum packed in modern, enamel-lined cans; stock rotation ensures absolute freshness. Farmer's Wife Milks, clinically proven to be digestible, nourishing and completely safe, meet the most rigid quality control standards. Available at all grocery and drug stores.

### **Farmer's Wife**

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**PORTAL HYPERTENSION IN CHINA**

Portal hypertension is a relatively common disease in China, with schistosomiasis as its main cause. Lan Hsi-Ch'un and his colleagues from Shanghai (*Chinese M. J.*, 76: 315, 1958) report the results of performing a shunt operation in 124 cases of portal hypertension, in half of which schistosoma ova were identified. Of the 124 patients 80% were males, and 63% had a past history of bleeding, while all had an enlarged spleen. Very few had ascites, which was considered a contraindication to the operation. In 95 cases a spleno-renal shunt was performed, in 27 a portacaval, and in 2 cases collateral and modified spleno-renal shunts were performed; portal pressure remained above normal immediately after operation, but slowly dropped to normal range. Coma developed after operation in 11 of the 27 cases of portacaval

(Continued on page 68)

For REAL PAIN—  
REAL RELIEF!



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Codeine  
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each tablet  
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Demerol hydrochloride 30 mg. (½ grain)

adult dose: 1 or 2 tablets repeated in three or four hours  
as needed.

supplied: Bottles of 100 and 1000 tablets, scored.  
Narcotic Blank Required.

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WINDSOR LABORATORIES OF CANADA LTD. ONTARIO

MEDICAL NEWS *in brief*

(Continued from page 66)

shunt but not in spleno-renal shunt, which the authors consider superior. There were 12 deaths—6 early and 6 late. To avoid mortality, the authors suggest that no case with persistent ascites or jaundice should be operated on, and the liver function must be fair. Bleeding from the upper gastro-intestinal tract developed in 5 cases after operation. The main cause of death was severe damage to the liver, which was not affected by operation, whereas bleeding could be dealt with effectively by surgery.

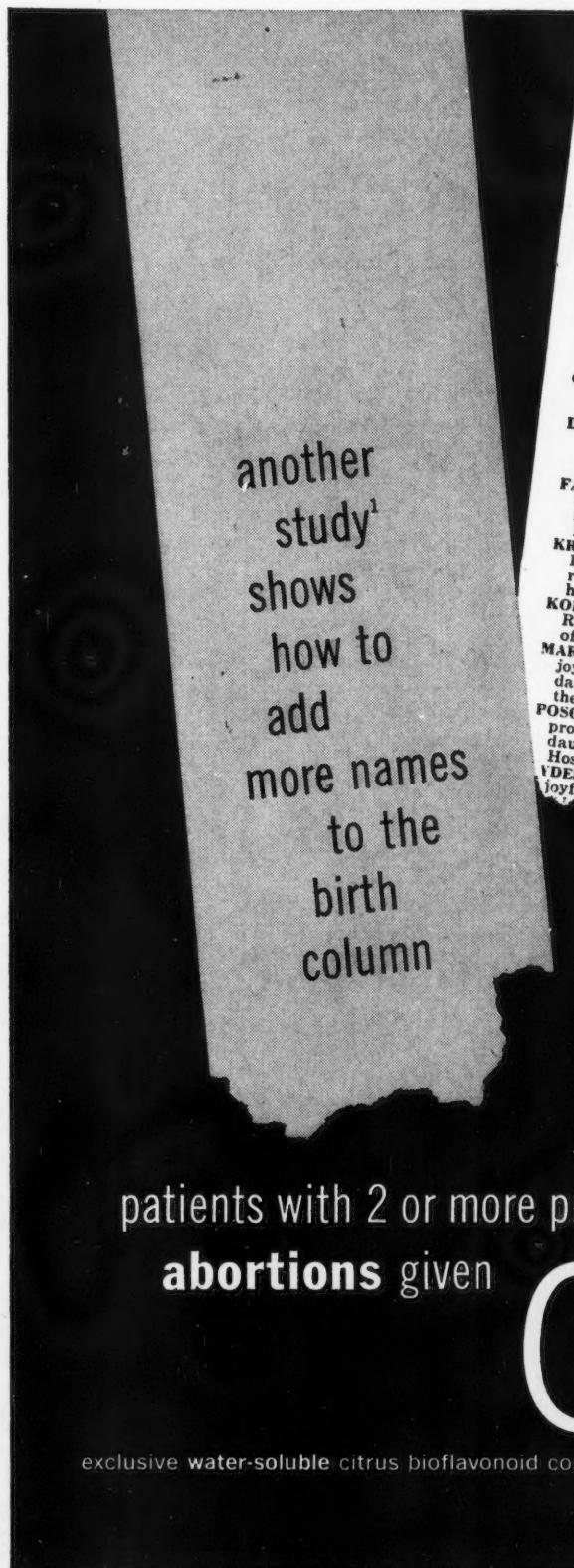
### SEDATION AND STIMULATION IN MAN

At a recent discussion at the Royal Society of Medicine in London on sedation and stimulation, Sargent (*Proc. Roy. Soc. Med.*, 51: 353, 1958) warned against placing too much reliance on the double-blind sampling method in evaluating new drugs. He deplored the tendency to lump too many psychiatric cases together in the testing of new tranquillizers, as it was more important to find out in which groups a tranquillizer such as chlorpromazine is better than Amytal, which is much cheaper and is still an effective drug in many conditions. Correct dosage is of paramount importance. He recalled the experiments of Pavlov in which the "strong excitatory" dog needed sometimes as much as eight times more of a sedative drug than the "weak inhibitory" dog. This observation has been confirmed in psychiatry in the various conditions as well as in the various types and constitutions of human beings. Whilst the bromides still have a field of usefulness in some tension states, the barbiturates are the best routine sedatives for the majority of neurotic patients. But one has to remember that chronic barbiturate poisoning can perpetuate a tension state. Addiction to longer-acting barbiturates is not as frequently observed as that to short-acting barbiturates, which are euphorants as well as more effective in relieving tension states. Chlorpromazine and meprobamate are particularly useful in psychotic patients although severe obsessional states are not generally helped by

these drugs. It may take one several years to learn how to use a new drug properly, and physicians should try to stick to a few drugs, both new and old, rather than play around ineffectively with too many. A short-acting barbiturate, a medium-acting one, and a long-acting one together with one or two of the new tranquillizers will prove a fairly satisfactory range of sedatives to use in clinical practice

for neurotic and normal patients. So far, stimulants have not been too effective and some addiction to them also is being seen. Amphetamine and allied drugs are ineffective in all but the mildest cases of depression. The newer substitutes such as phenmetrazine (Preludin) and pipradol (Meratran) have fewer side effects than amphetamine.

Later in the discussion, Wayne



### Births

**BASSAK**—Mr. and Mrs. Robert Bassak joyfully announce the arrival of Jill's sister, Wendy, August 23, at Beth Israel Hospital.

**BLUMBERG**—Mel and Susan joyfully announce the arrival of their son Joel Marc, August 21, 1957.

**COX**—Mr. and Mrs. David J. Cox announce the arrival of their son, Harvey, brother of Linda and Stuart, August 17, 1957.

**CHASTINE**—Arthur and Ellen happily announce the birth of Lisa Jane in Los Angeles, California, August 21, 1957.

**DEWAR**—Lieut. and Mrs. Jonathan Dewar announce the birth of their son Allen Jay, August 18, at Klingenstein Pavilion.

**FARRANT**—Richard and Kay (nee Gower) of Riverdale, New York, proudly announce the birth of their second son Barry James, August 22, 1957.

**KROGH**—Mr. and Mrs. Felix Krogh (nee Lehrer) are happy to announce the arrival of their son Erik, at the Guggenheim Pavilion, August 22.

**KOENIG**—The Koenigs, Louis, Pamala (nee Rehr) and Erwin announce the arrival of Kenneth Alan, on August 18, 1957.

**MARLOW**—Mr. and Mrs. Ramsey Marlow joyfully announce the arrival of their daughter Chris on August 22, 1957 at the Mt. Sinai Hospital.

**POSON**—Mr. and Mrs. Michael Poson proudly announce the arrival of their daughter Jeannine Beth, at Doctors Hospital, on August 20, 1957.

**RIDER**—Mr. and Mrs. Martin B. Ryder joyfully announce the birth of their son

**WILSON**—Lawrence and Charles, August 21, 1957.

reviewed the pharmacological background and possible action of the tranquilizing drugs. No clear-cut statements regarding the mechanism by which these drugs produce their effect on the central nervous system can be made, but there is some evidence that acetylcholine, noradrenaline and 5-hydroxytryptamine(5HT) may all play a part in central transmission, and that the tranquilizing drugs

interfere with one or the other of these substances. From three careful clinical trials, Wayne drew the conclusion that meprobamate is a moderately active sedative of no greater clinical value than amylobarbitone or phenobarbitone. When allowance is made for the 35% of any population which respond favourably to any form of therapy including inert tablets there is, according to work quoted,

little evidence that this group of tranquilizers includes many very active drugs. When they are active, they do not appear to be greatly preferable to the conventional barbiturates in the treatment of neuroses. Among the stimulants there is little to choose between the older and the newer preparations, although some of the new compounds such as pipradol may have fewer side effects. Mixtures of sedative and stimulant drugs do not completely cancel out each other's effects and their use may have some logic. The objection to their use is that they are rarely mixed in proportions which will suit every case and they are especially liable to cause addiction.

### capillary fault frequently responsible

Noting the frequency with which the capillary syndrome causes habitual abortion, Pearse and Trisler<sup>1</sup> administered capillary-corrective C.V.P. to 25 pregnant women with two or more previous spontaneous abortions.

### C.V.P...useful corrective

Nineteen (76 per cent) "delivered living babies." Normal delivery was preceded by a complete arrest of bleeding, which in previous abortions was clearly manifested. "It appears that the prenatal death rate may be considerably decreased by restoration of capillary integrity and that the bioflavonoids offer a useful therapeutic agent."

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1. Pearse, H. A. and Trisler, J. D.: Clinical Med. 4:1081, 1957.

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### 1-PHENYL-2-AMINOPROPANE ALGINATE (LEVONOR), NEW ANORECTIC

According to Gadek *et al.* (J. A. M. A., 167: 433, 1958), Levonor has been shown in animal and in clinical studies to be superior to the older drugs for causing anorexia. It produced pronounced anorexia without the undesirable side effects of hyperexcitability, insomnia, weakness and depression.

Their own studies on a group of 80 overweight patients, ranging in age from 15 to 69 years, confirmed that Levonor was a highly satisfactory anorectic. In preliminary studies in which placebos were compared with this drug in a double-blind test, they found that patients on a diet plus the drug lost approximately 1.8 times the weight per week lost by the group on diet plus a placebo.

A comprehensive approach is needed to weight reduction in each patient, with careful physical examination, explanation and encouragement as well as frequent check-ups, at which times additional education and encouragement are given. Follow-up after weight loss is another very important factor in maintaining the desirable weight, and the patient is advised to see his physician if weight gain is over 5 lb. In 3 cases presented in detail, this management plus 5 mg. Levonor three times daily produced excellent results. In a fourth case the patient lost weight satisfactorily with the drug, but missed the "lift" previously experienced with amphetamine preparations.

stop  
“morning  
sickness”  
the  
night  
before  
with  
timed-  
release  
**Bendectin**  
2 tabs. h.s.



**PREVENTS “MORNING SICKNESS” IN 9 OUT OF 10 PREGNANCIES**

In 941 cases<sup>1,2</sup> effective in all but 17. Two timed-release tablets at bedtime start to work in the early morning and reach maximum potency at normal waking hour. BENDECTIN then provides exceptional relief of nausea and vomiting by three distinct and complementary actions. 1. Antispasmodic—Bentylol 10 mg.—relaxes G-I smooth-muscle spasm; 2. Antinauseant—Decapryl 10 mg.—centrally effective . . . combats histamine-like metabolites often present in blood stream during pregnancy; 3. Nutritional supplement—pyridoxine 10 mg.—just the amount necessary to help control “morning sickness.”

1. Nulsen, R. O.: Ohio State M. J. 53:665, 1957. 2. Personal communications, 1956-57.



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